David Gozal, MD, MBA, PhD

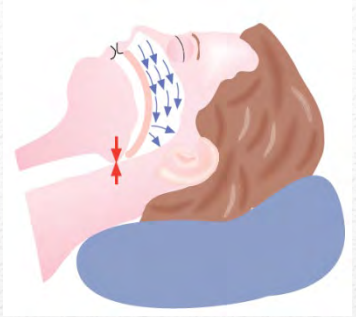
Professor and Dean
Vice President Health Affairs

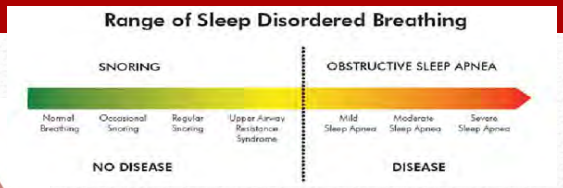
Snoring Child: Evaluation and Diagnosis

MARSHALL UNIVERSITY®
Joan C. Edwards School of Medicine

Consequences

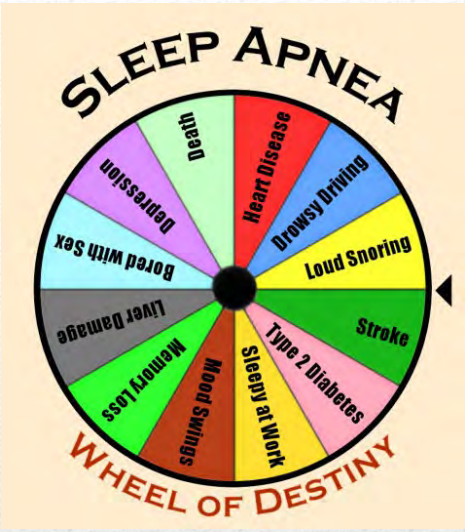
APNEA **NORMAL**

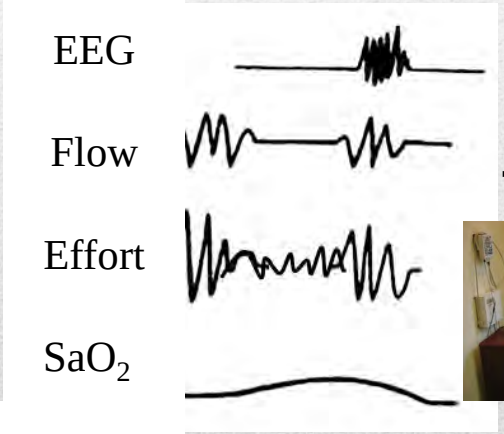




OSAS
Adults
4-6%
Children
1-3%

Sleepiness
Cardiovascular
Stroke
Metabolic
Neurocognitive
Depression
MVA
Erectile Dysfunction
Cancer…





OSA
Adults
15-20%
Children
6-12%

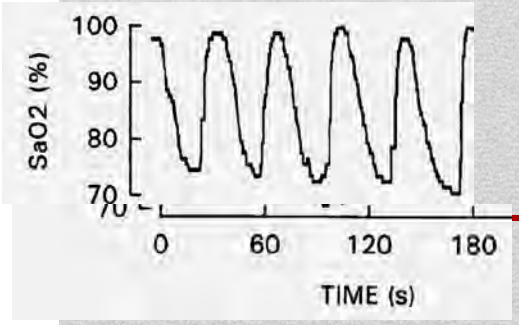
Arousals

↑ **Intrathoracic Pressures**

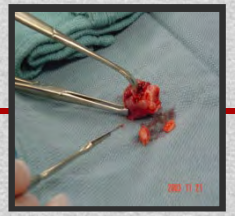
CO_2

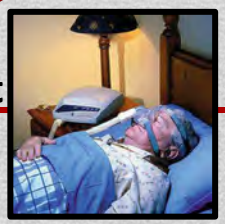
Hypoxemia

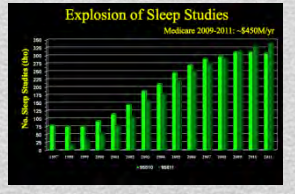
Autonomic activity
Hemodynamic changes
Hypercoagulability
Inflammation
Oxidative Stress



Treatment







How do we diagnose a child with obstructive sleep apnea?

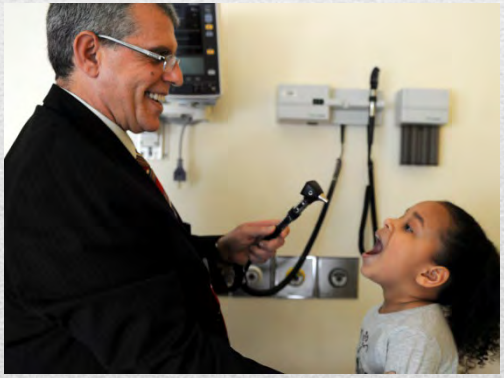
- Feeling sleepy during day
- Snoring loud
- Stop breathing during sleep
- Morning headaches
- Behavioral issues
- Bed wetting
- Parasomnias (nightmares, night terrors,..)
- Bruxism
- Mood swings
- Asthma
- Recurrent otitis media
- Mouth breathing

Snore +

Who needs a study?

Evaluation in sleep clinic

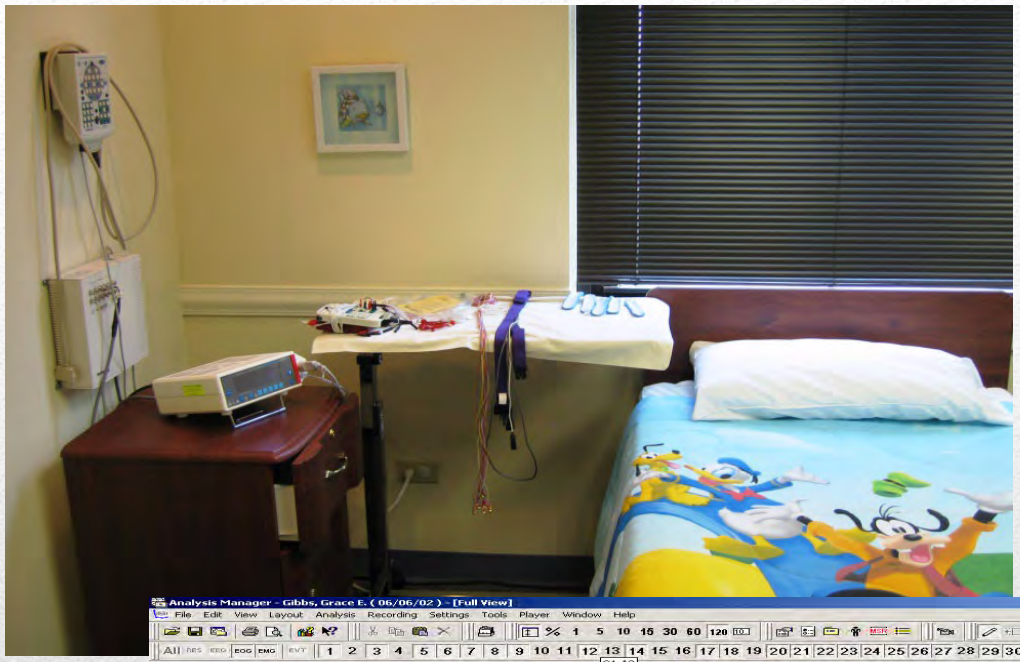
- Symptoms in children might be different than adults
- Getting a good history from the patient is very important
- Physical exam
- Questionnaires

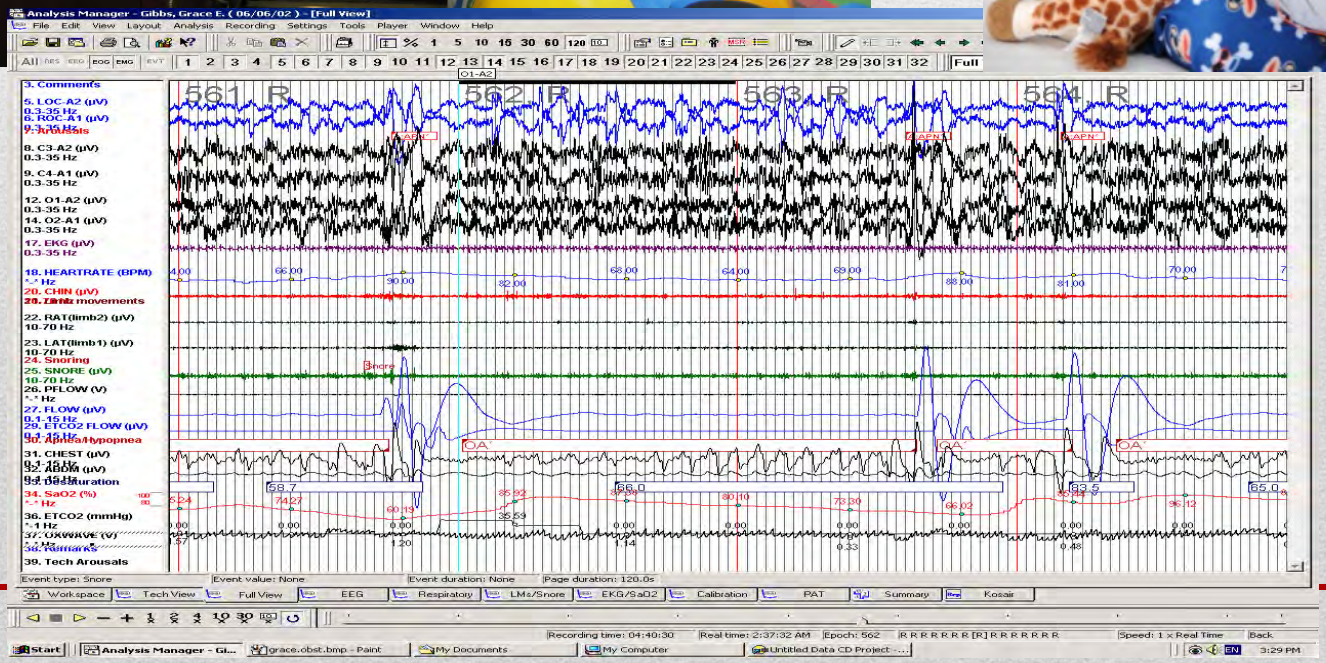


PSG - The Gold Standard

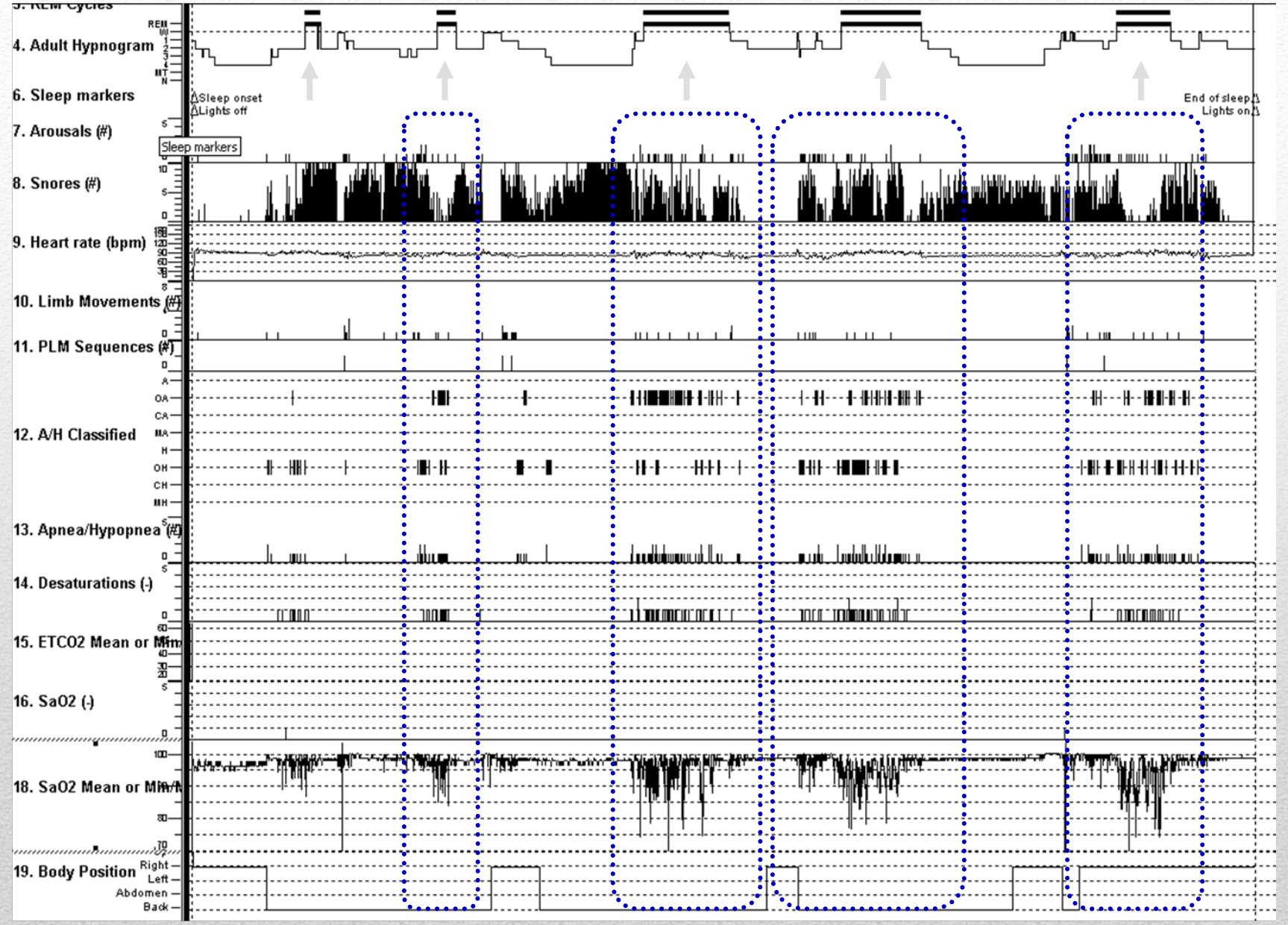

OK, NOW JUST SLEEP NORMALLY...
SLEEP STUDY

Current diagnostic test: Polysomnography





Marcus et al, Pediatrics 2012; 130(3):576-84.


4. Adult Hypnogram
6. Sleep markers
Sleep onset
Lights off
End of sleep
Lights on
7. Arousals (#)
Sleep markers
8. Snores (#)
9. Heart rate (bpm)
10. Limb Movements (#)
11. PLM Sequences (#)
12. A/H Classified
13. Apnea/Hypopnea (#)
14. Desaturations (-)
15. ETCO2 Mean or Min
16. SaO2 (-)
18. SaO2 Mean or Min
19. Body Position
Right
Left
Abdomen
Back

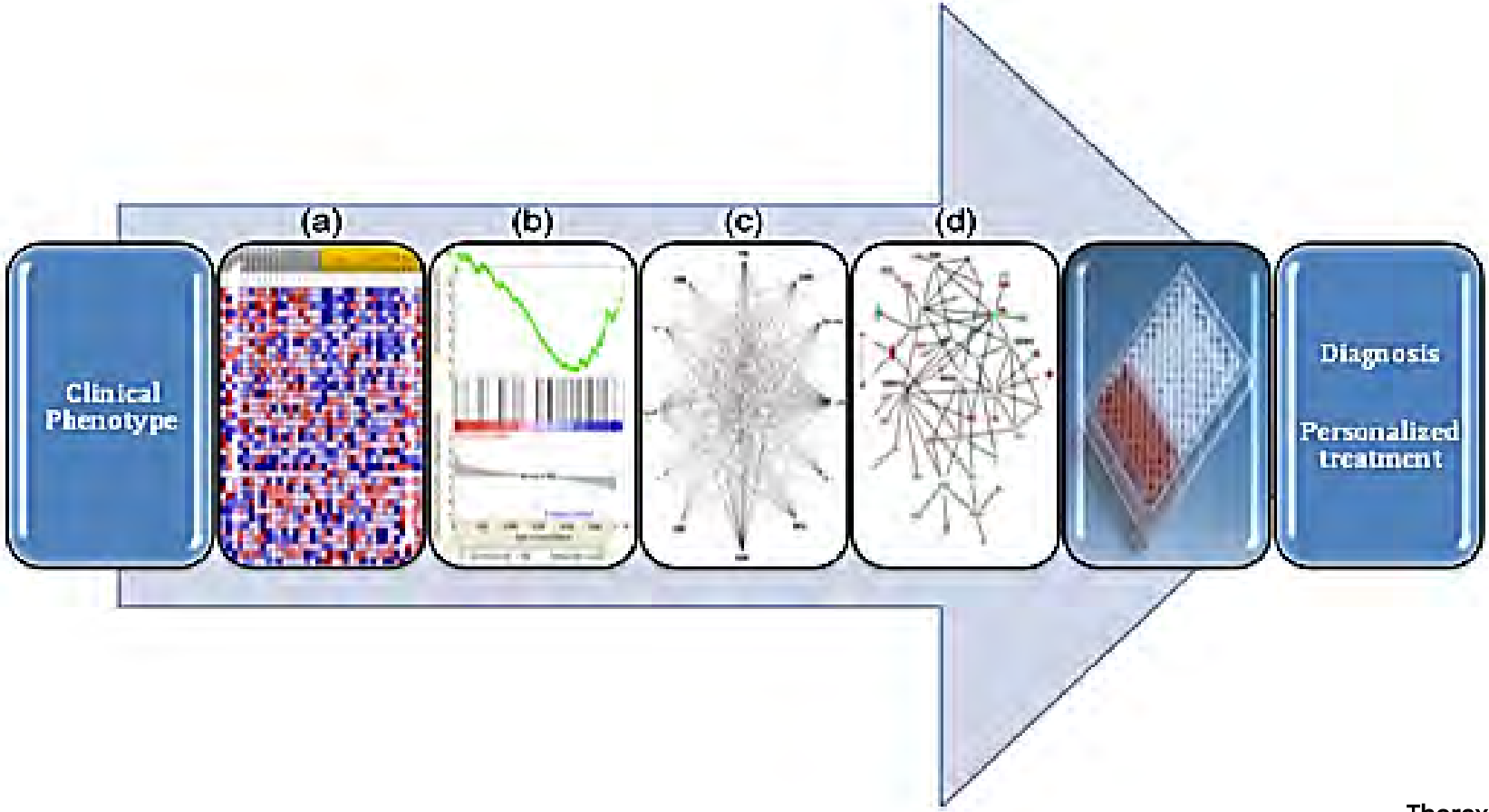
The Gold Standard gives us many things but
we really use only one to diagnose OSA:

	Normal	Mild-moderate	Moderate	Severe
Child	AHI <1	1<AHI<5	5<AHI<10	AHI>10
Adult	AHI <5	5<AHI<15	15<AHI<30	AHI>30

Not enough pediatric sleep specialists to diagnose all the kids at risk of SDB!!!

The promise of translational and personalised approaches for paediatric obstructive sleep apnoea: an 'Omics' perspective

Hui-Leng Tan,[1] Leila Kheirandish-Gozal,[2] David Gozal[2]



Thorax, 2014

History and Physical

Inability of Clinical History to Distinguish Primary Snoring From Obstructive Sleep Apnea Syndrome in Children*

John L. Carroll, MD; Susanna A. McColley, MD; Carole L. Marcus, MBBCh; Shelly Curtis, RN; and Gerald M. Loughlin, MD

Our data indicate that the clinician (including pediatric pulmonologists, otolaryngologists, and plastic surgeons) evaluating a child with snoring cannot, at the present time, reliably distinguish PS from OSA without some type of measurement of breathing during sleep.

CHEST Original Research
SLEEP DISORDERS

Screening of Pediatric Sleep-Disordered Breathing

A Proposed Unbiased Discriminative Set of Questions Using Clinical Severity Scales

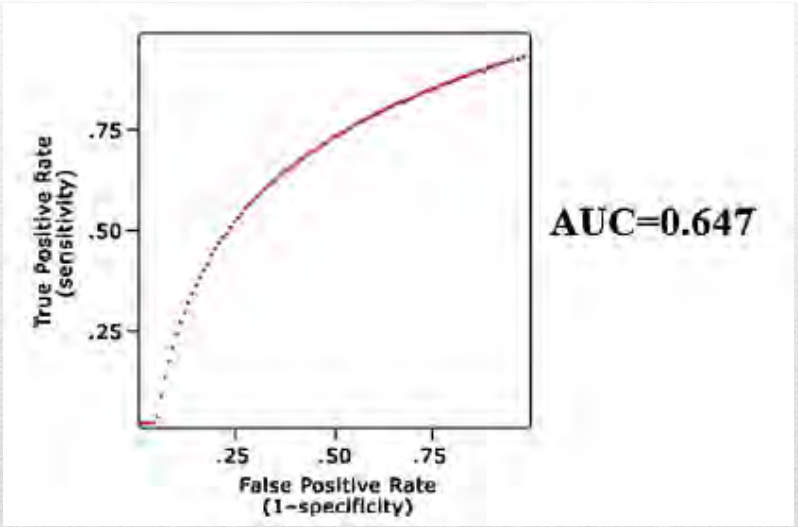
Karen Spruyt, PhD; and David Gozal, MD, FCCP

Contents lists available at SciVerse ScienceDirect
International Journal of Pediatric Otorhinolaryngology
journal homepage: www.elsevier.com/locate/ijporl

Validation of a pediatric obstructive sleep apnea screening tool

Gili Kadmon [a,*], Colin M. Shapiro [b], Sharon A. Chung [b], David Gozal [c]

[a] Pediatric Intensive Care Unit, Schneider Children's Medical Center (Affiliated with Sackler Faculty of Medicine, Tel-Aviv University), Israel
[b] Youthdale Child and Adolescent Sleep Centre, Canada
[c] Department of Pediatrics and Comer Children's Hospital, Pritzker School of Medicine, the University of Chicago, Chicago, IL, United States



Sleep Medicine 30 (2017) 24–28
Contents lists available at ScienceDirect
Sleep Medicine
journal homepage: www.elsevier.com/locate/sleep

Original Article

Performance characteristics of the French version of the severity hierarchy score for paediatric sleep apnoea screening in clinical settings

Xuân-Lan Nguyên [a,*], Pierre Lévy [b], Nicole Beydon [c], David Gozal [d], Bernard Fleury [a]

Using 6 questions based on:

Spruyt and Gozal, CHEST 2012; 142:1508-15.

A cumulative score $\geq$2.8 leads to a sensitivity of 83%, specificity of 64%, PPV of 28% and NPV of 96%

Questionnaires

Subject ID:

Age			Date of Birth		
Sex	Male		Race & Ethnicity	White	Non-Hispanic
	Female			African American	Hispanic
Weight	Lbs	Kg		Asian	
Height	Ft	Inch		Alaska Native / American Indian	
	Cm			More than one race	

Please answer to the following questions considering your child's sleep during past 6 months

	Never	Rarely (once per week)	Occasionally (twice per week)	Frequently (3-4 times per week)	Almost Always (more than 4 times per week)
Does your child stop breathing during sleep?					
Does your child struggle to breathe while sleep?					
Do you ever shake your child to make him/her breathe again when sleep?					
How often does your child snore?					
Do you have any concerns about your child's breathing while asleep?					
How loud does your child snore?	Mildly Quiet	Medium Loud	Loud	Very Loud	Extremely Loud

Sleep Medicine 30 (2017) 24–28

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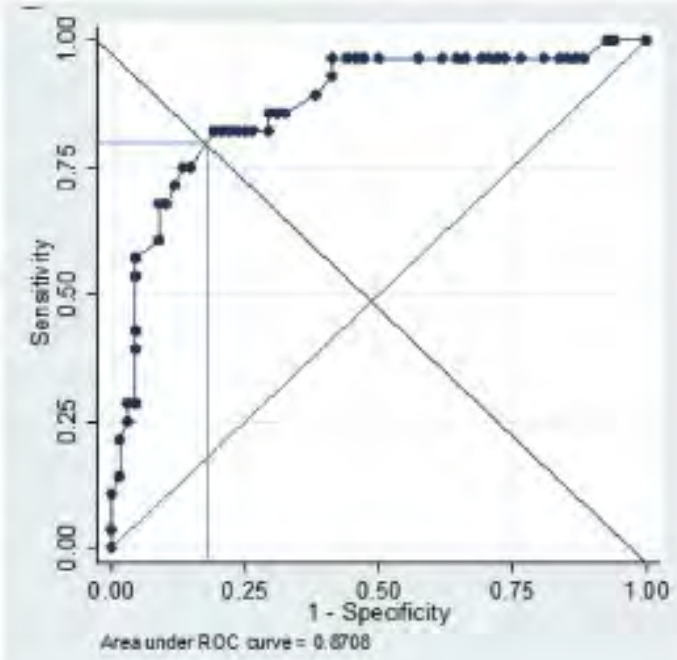
Xuân-Lan Nguyên [a, *], Pierre Lévy [b], Nicole Beydon [c], David Gozal [d], Bernard Fleury [a]



Using 6 questions based on:

Spruyt and Gozal, CHEST 2012; 142:1508-15.

Table 3
Cut-off value for the severity hierarchy score yielding optimal prediction of obstructive sleep apnoea syndrome (AHI ≥ 5/hrTST).

SHS value	Sensitivity (%)	Specificity (%)	PPV (%)	PVN (%)
2.75	82.1	80.9	63.9	91.7
95% CI	74.4–89.8	73.0–88.8	54.3–73.5	86.2–97.2

Abbreviations: SHS, severity hierarchy score; PPV, positive predictive value; NPV, negative predictive value; CI, confidence intervals.

International Journal of Pediatric Otorhinolaryngology 113 (2018) 62–66

Contents lists available at ScienceDirect

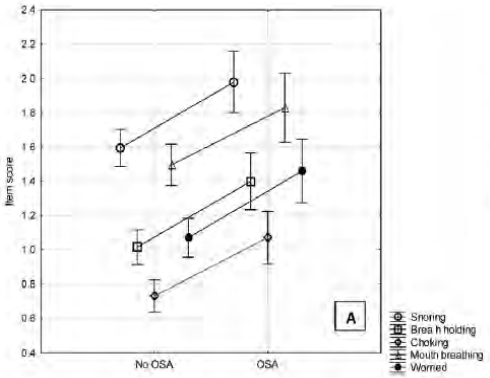
International Journal of Pediatric Otorhinolaryngology

journal homepage: www.elsevier.com/locate/ijporl

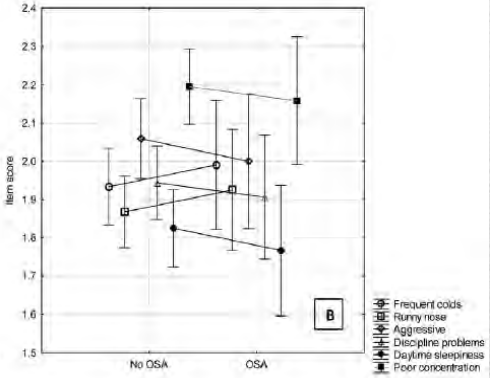
The OSA-5: Development and validation of a brief questionnaire screening tool for obstructive sleep apnea in children☆

Han Jie Soh[a], Katherine Rowe[b], Margot J. Davey[a,c], Rosemary S.C. Horne[a], Gillian M. Nixon[a,c,*]

PSG



Oximetry



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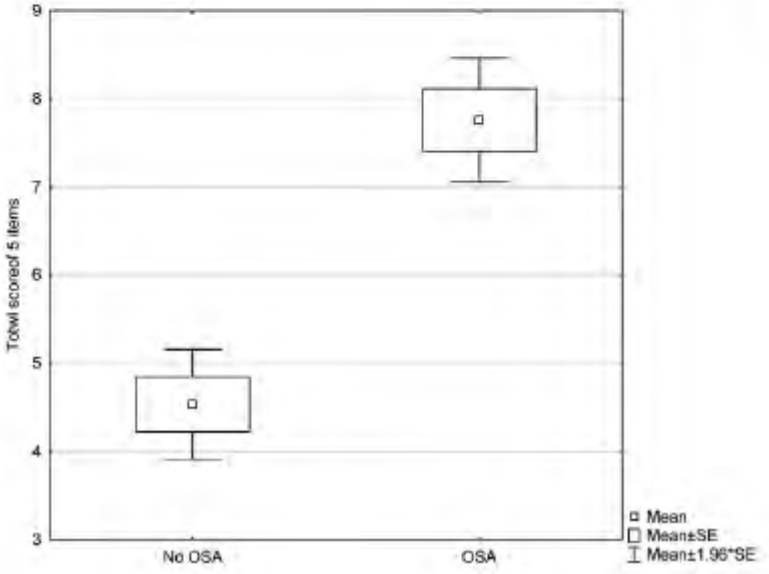
Han Jie Soh[a], Katherine Rowe[b], Margot J. Davey[a,c], Rosemary S.C. Horne[a], Gillian M. Nixon[a,c,*]

For detection of OSA (OAHI>1event/h) using a threshold of a total score greater than or equal to 5/15 for the 5 questions, sensitivity is 46/ 58 (79%) and negative predictive value 19/31 (61%), with specificity of 19/54 (35%) and positive predictive value of 46/81 (57%).

For detection of moderate/severe OSA (OAHI≥5events/h), the sensitivity is 27/33 (82%) and negative predictive value 25/31 (81%), however, the specificity remains low at 25/79 (32%) and positive predictive value is also low at 27/81 (33%).

Table 1
The 5-question instrument (OSA-5) developed during the study and tested for prediction of OSA in the prospective validation phase of the project.

	During the past 4 weeks, how often has your child had ...	None of the time	Some of the time	Most of the time	All of the time
1	Loud snoring?	0	1	2	3
2	Breath holding spells or pauses in breathing at night?	0	1	2	3
3	Choking or made gasping sounds while asleep?	0	1	2	3
4	Mouth breathing because of a blocked nose?	0	1	2	3
5	Breathing problems during sleep that made you worried that they were not getting enough air?	0	1	2	3



Too many proposals

Contents lists available at ScienceDirect

Sleep Medicine

journal homepage: www.elsevier.com/locate/sleep

Original Article

TuCASA questionnaire for assessment of children with obstructive sleep apnea: validation

Jacqueline Maria Resende Silveira Leite [a], Vanessa Ruotolo Ferreira [b], Lucila Fernandes do Prado [b], Gilmar Fernandes do Prado [b], José Fausto de Morais [c], Luciane Bizari Coin de Carvalho [a,b,*]

International Journal of Pediatric Otorhinolaryngology 77 (2013) 1864–1868

Contents lists available at ScienceDirect

International Journal of Pediatric Otorhinolaryngology

journal homepage: www.elsevier.com/locate/ijporl

Questionnaire OSA-18 has poor validity compared to polysomnography in pediatric obstructive sleep apnea

Anna Borgström *, Pia Nerfeldt, Danielle Friberg

reinforce the concept that

International Journal of Pediatric Otorhinolaryngology 95 (2017) 139–144

Contents lists available at ScienceDirect

International Journal of Pediatric Otorhinolaryngology

journal homepage: http://www.ijporlonline.com/

Clinical symptoms that predict the presence of Obstructive Sleep Apnea

Kevin C. Lewis [a], James W. Schroeder Jr. [b, c], Bushra Ayub [b], Bharat Bhushan [b, c, *]

no single tool is good enough

International Journal of Pediatric Otorhinolaryngology 78 (2014) 2116–2120

Contents lists available at ScienceDirect

International Journal of Pediatric Otorhinolaryngology

journal homepage: www.elsevier.com/locate/ijporl

I'M SLEEPY: A short pediatric sleep apnea questionnaire

Gili Kadmon [a,*], Sharon A. Chung [b], Colin M. Shapiro [b]

Diagnostic capability of questionnaires and clinical examinations to assess sleep-disordered breathing in children

A systematic review and meta-analysis

Graziela De Luca Canto, DDS, MSc, PhD; Vandana Singh, DDS, MSc; Michael P. Major, DMD, MSc, FRCD; Manisha Witmans, MD, FRCPC; Hamdy El-Hakim, MD, FRCS(Ed), FRCS(ORL-HNS); Paul W. Major, DDS, MSc, FRCD(C); Carlos Flores-Mir, DDS, DSc, FRCD(C)

JADA 2014;145(2):165-178.

A. Questionnaire

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Yang and Colleagues,[38] 2010	19	16	9	19	0.68 (0.48-0.84)	0.54 (0.37-0.71)
Chan and Colleagues,[40] 2012	14	33	14	41	0.50 (0.31-0.69)	0.55 (0.43-0.67)
Chervin and Colleagues,[21] 2000	56	2	13	10	0.81 (0.70-0.90)	0.83 (0.52-0.98)

B. Questionnaire and Physical Examination

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Goldstein and Colleagues,[1] 2012	51	11	15	17	0.77 (0.65-0.87)	0.61 (0.41-0.78)
Li and Colleagues,[48] 2006	50	32	16	131	0.76 (0.64-0.85)	0.80 (0.73-0.86)
Sproson and Colleagues,[52] 2009	26	26	12	14	0.68 (0.51-0.82)	0.61 (0.39-0.80)

C. Questionnaire and Physical Examination and Other Tests

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Chervin and Colleagues,[51] 2007	32	18	9	46	0.78 (0.62-0.89)	0.72 (0.59-0.82)
Goldstein and Colleagues,[50] 1994	12	12	1	5	0.92 (0.64-1.00)	0.29 (0.10-0.56)
Lamm and Colleagues,[24] 1999	5	2	6	10	0.45 (0.17-0.77)	0.83 (0.52-0.98)
Yang and Colleagues,[43] 2012	229	34	135	129	0.63 (0.58-0.68)	0.79 (0.72-0.85)

D. Physical Examination and Other Tests

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Supriyatno and Colleagues,[10] 2010	26	0	16	68	0.62 (0.46-0.76)	1.00 (0.95-1.00)

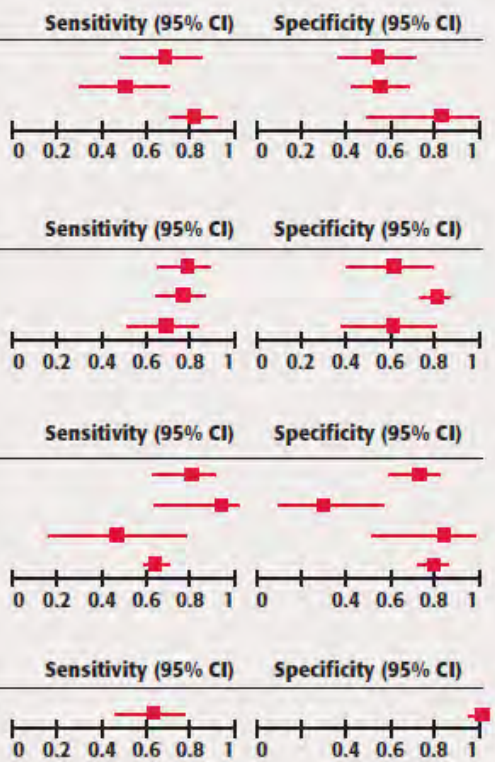


Figure 2. Forest plot with the diagnostic accuracy (sensitivity, specificity and 95 percent confidence interval) of each study. TP: True positive. FP: False positive. FN: False negative. TN: True negative. CI: Confidence interval.

Diagnostic capability of questionnaires and clinical examinations to assess sleep-disordered breathing in children

A systematic review and meta-analysis

Graziela De Luca Canto, DDS, MSc, PhD; Vandana Singh, DDS, MSc; Michael P. Major, DMD, MSc, FRCD; Manisha Witmans, MD, FRCPC; Hamdy El-Hakim, MD, FRCS(Ed), FRCS(ORL-HNS); Paul W. Major, DDS, MSc, FRCD(C); Carlos Flores-Mir, DDS, DSc, FRCD(C)

JADA 2014;145(2):165-178.

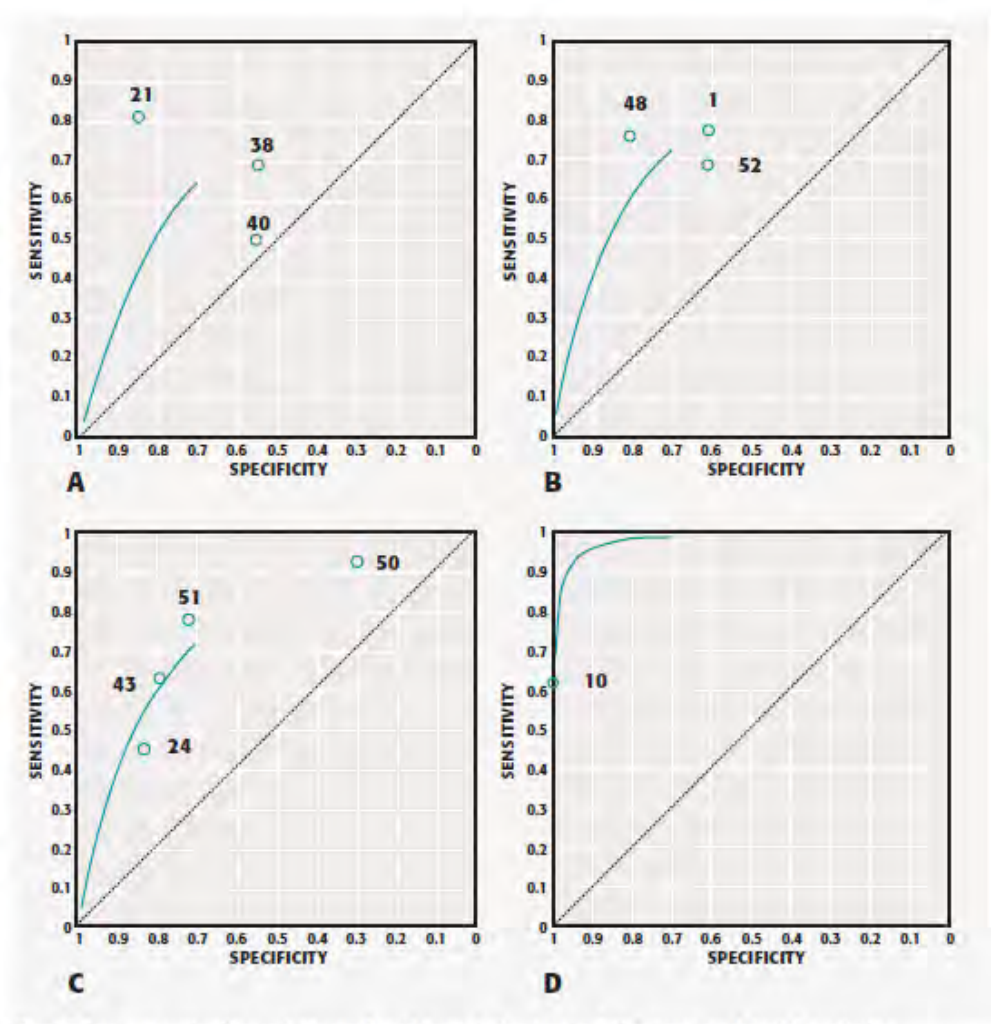
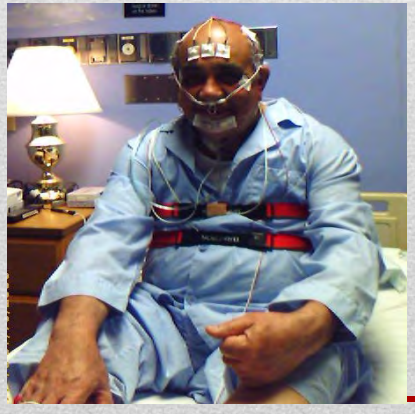


Figure 3. Receiver operating characteristic curves for each group. **A.** Questionnaire. **B.** Questionnaire and physical examination. **C.** Questionnaire and physical examination and other test. **D.** Physical examination and other test. The numbers in the graphs refer to the articles' reference numbers.

Sleep Center	Home		
Type I	**Type II**	**Type III**	**Type IV**
Attended studies are performed with the oversight of a sleep technologist with full sleep staging with the use of EEG electrodes	Home sleep test (HST) with Type II portable Monitor unattended (sleep studies that are performed without the oversight of a sleep technologist), with a minimum of 7 channels.	Home sleep test (HST) with Type III portable monitor, unattended with a minimum of 4 channels.	Home sleep test (HST) with Type IV portable monitor, unattended; minimum of 3 channels.
Must include the following channels: ▪EEG ▪EOG ▪ECG/Heart rate ▪Chin EMG ▪Limb EMG ▪Respiratory effort at thorax and ▪abdomen ▪Air Flow from nasal canula thermistor ▪and/or X-Flow	Must include the following channels: ▪EEG ▪EOG ▪ECG/heart rate ▪EMG ▪Airflow ▪Respiratory effort ▪Oxygen saturation	Must include the following channels: ▪2 respiratory movement/airflow ▪1 ECG/heart rate ▪1 oxygen saturation	Must allow channels that allow direct calculation of an AHI or RDI as the result of measuring airflow or Thoraco-abdominal movement.
			

SCOPER Categories, From Collop et al[20]

Sleep	Cardiovascular	Oximetry	Position	Effort	Respiratory
S1: Sleep by 3 EEG channels (frontal, central, occipital) with EOG and chin EMG	C1: >1 ECG lead	O1: Oximetry (finger/ear) with recommended sampling (ie, 3-s averaging and a minimum 10-Hz sampling rate)	P1: Video or visual position measurement	E1: 2 RIP bands	R1: Nasal pressure transducer and thermistor
S2: Sleep by <3 EEG with or without EOG or chin EMG	C2: Peripheral arterial tonometry	O1x: Oximetry (finger/ear) that does not fulfill recommended sampling (or if sampling not stated)	P2: Nonvisual position measurement	E2: 1 RIP band	R2: Nasal pressure transducer
S3: Sleep surrogate such as actigraphy	C3: 1 ECG lead	O2: Oximetry from alternate site (eg, forehead)	...	E3: Derived effort	R3: Thermistor
S4: Other sleep measure	C4: Derived pulse (usually from oximetry)	O3: Other oximetry	...	E4: Other effort measure (including piezo bands)	R4: End-tidal CO_2
...	C5: Other cardiac measure	...	...	...	R5: Other respiratory measure

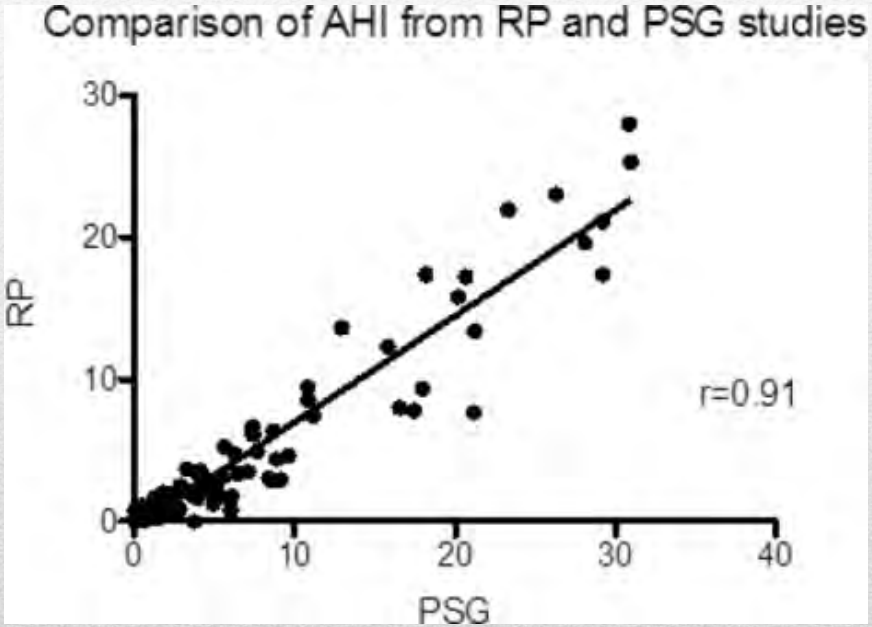
Collop NA, Tracy SL, Kapur V, et al. Obstructive sleep apnea devices for out-of-center (OOC) testing: technology evaluation. *J Clin Sleep Med.* 2011;7(5):531-548.

PSG VERSUS RESPIRATORY POLYGRAPHY IN THE DIAGNOSIS OF PEDIATRIC OSA

http://dx.doi.org/10.5665/sleep.3392

Overnight Polysomnography versus Respiratory Polygraphy in the Diagnosis of Pediatric Obstructive Sleep Apnea

Hui-Leng Tan, MD[1,2]; David Gozal, MD[1]; Helena Molero Ramirez, MD[1]; Hari P. R. Bandla, MD[1]; Leila Kheirandish-Gozal, MD, MSc[1]

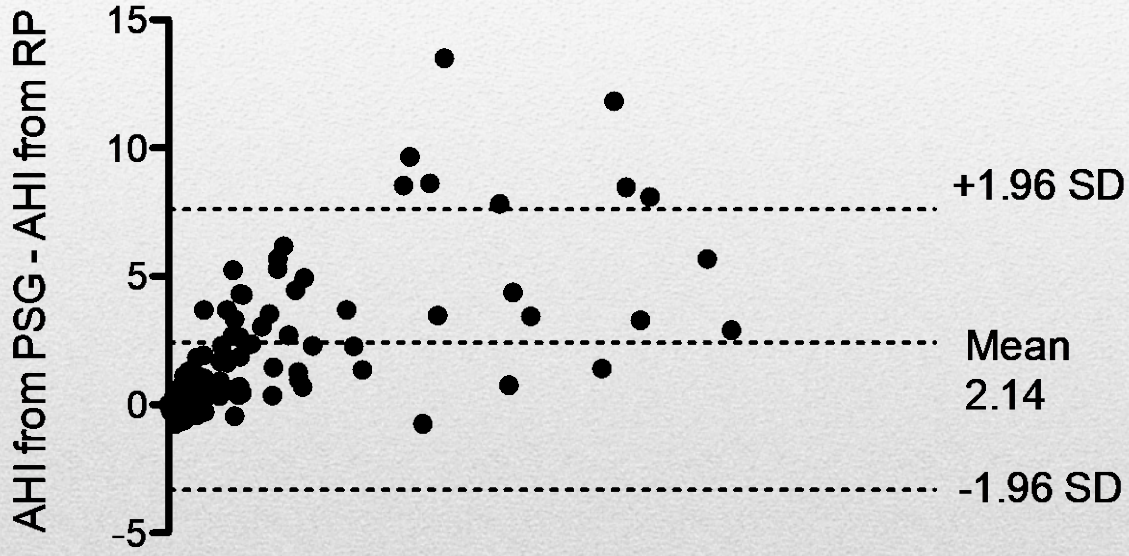


Great correlation between PSG and RP in the sleep laboratory

Respiratory Polygraphy Rather Than Polysomnography

SLEEP 2014;37(2):255-260

Polygraphy Rather Than Polysomnography



AHI is underestimated in RP, and the disparity in AHI-RP and AHI-PSG can significantly affect clinical management decisions, particularly in children with mild and moderate OSA (1<AHI<10/hrTST).

Tan et al, SLEEP 2014;37:255-60

International Journal of Pediatric Otorhinolaryngology 100 (2017) 44–51

Contents lists available at ScienceDirect

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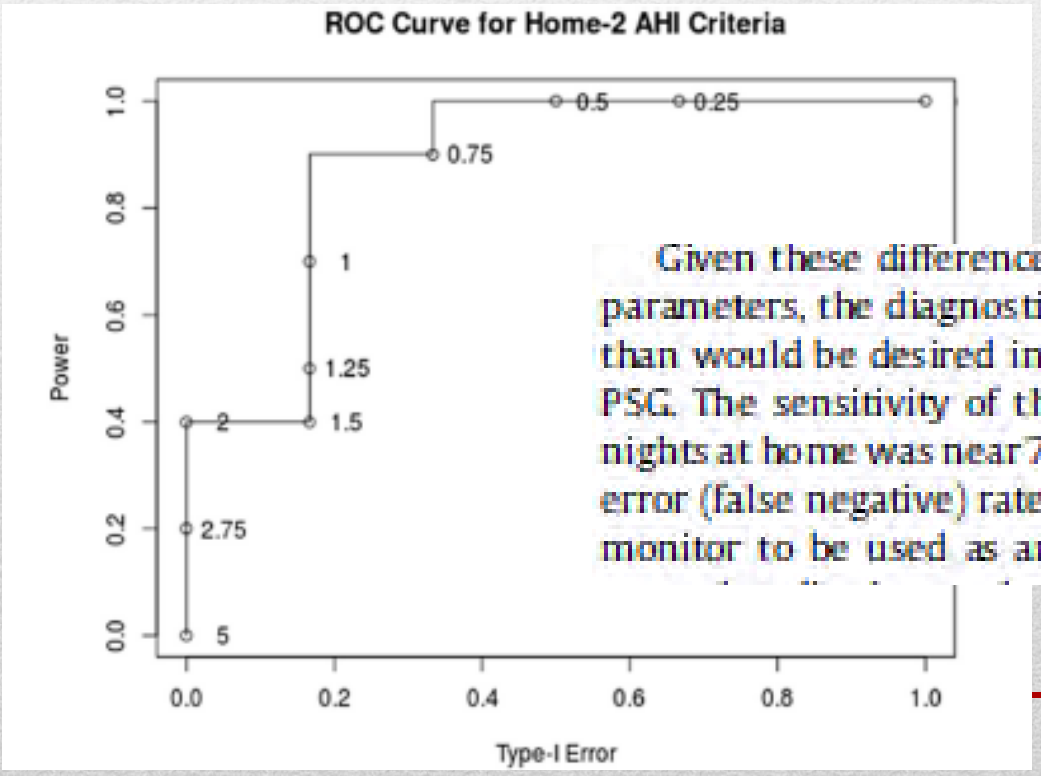
journal homepage: http://www.ijporlonline.com/

Comparison of home sleep apnea testing versus laboratory polysomnography for the diagnosis of obstructive sleep apnea in children

Nicholas Scalzitti [a, *], Shana Hansen [b], Stephen Maturo [a], Joshua Lospinoso [c], Peter O'Connor [a, b]



Given these differences in the measurement of the respiratory parameters, the diagnostic ability of the portable monitor was less than would be desired in order for the home study to replace the PSG. The sensitivity of the monitor for diagnosing OSA for the 2 nights at home was near 70% for each use. However, the 30% Type-II error (false negative) rate associated with this would preclude the monitor to be used as an accurate screening test for OSA in the

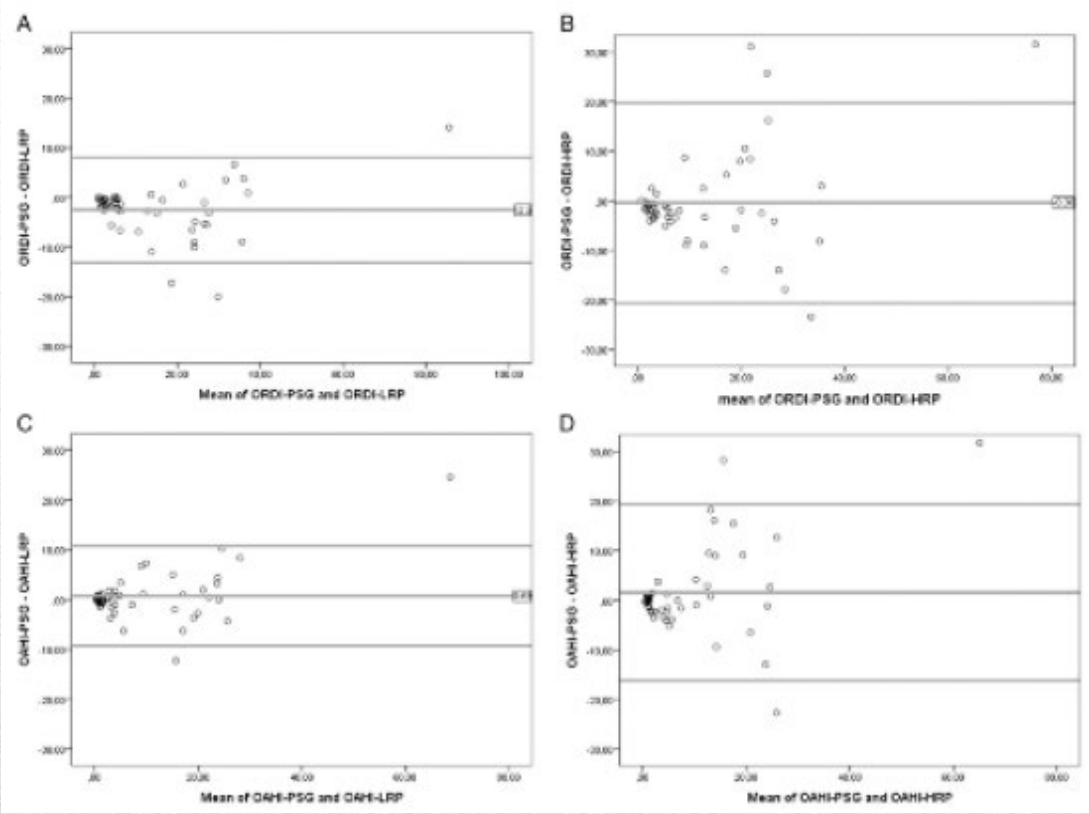
Only 20 subjects

AHI is underestimated in HRP, the optimal AHI-HRP corresponding to the PSG-defined OSAS criterion was established as **> 5.6 / h.** The latter exhibited a **sensitivity of 90.9%** (95% CI, 79.6%-100%) and a **specificity of 94.1%** (95% CI, 80%-100%).

TABLE 3] ICCs and 95% CIs for Several Respiratory Cutoff Values Used as OSAS Diagnostic Criteria

PSG	LRP	HRP
RDI ≥ 3	96 (91.8-97.9)	85.9 (75.2-92)
ORDI ≥ 3	96.5 (92.3-98.2)	86.7 (76.5-92.5)
OAHI ≥ 3	95.8 (92.6-97.6)	84.3 (72.5-91.1)

Data are presented as ICC (95% CI), %. ICC = intraclass correlation coefficient; OSAS = OSA-hypopnea syndrome. See Table 1 and 2 legends for expansion of other abbreviations.



Home Polygraphy Rather Than Polysomnography?

Reliability of Home Respiratory Polygraphy for the Diagnosis of Sleep Apnea in Children

María Luz Alonso-Álvarez, MD; Joaquin Terán-Santos, MD; Estrella Ordax Carbajo, MD, PhD; José Aurelio Cordero-Guevara, MD; Ana Isabel Navazo-Egüia, MD; Leila Kheirandish-Gozal, MD; and David Gozal, MD, FCCP

CHEST 2015; 147(4):1020-1028

International Journal of Pediatric Otorhinolaryngology 94 (2017) 54–58

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Comparison of diagnostic reliability of out-of-center sleep tests for obstructive sleep apnea between adults and children

Masaaki Suzuki [a,*], Taiji Furukawa [b], Akira Sugimoto [a], Ryosuke Kotani [a], Rika Hosogaya [a]

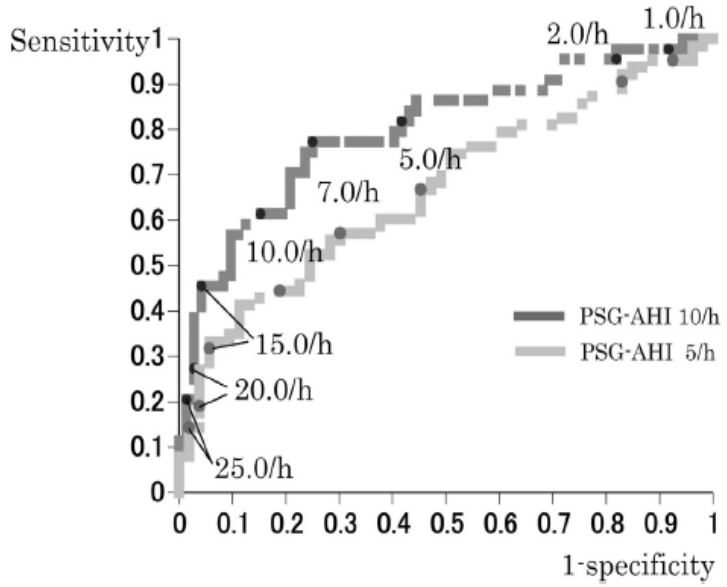
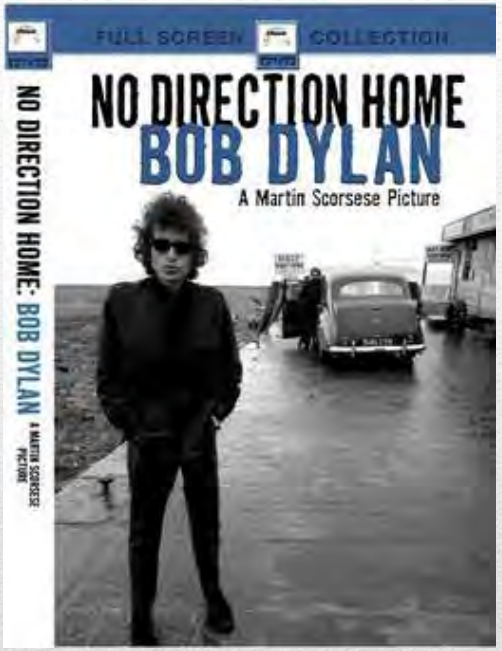


Fig. 2. ROC curves of PSG-AHI 10/h and 5/h for children. ODI 7.0/h was the cutoff point at the highest accuracy for PSG-AHI 10/h and 5/h. The AUCs of PSG-AHI 10/h and 5/h for children were 0.80 and 0.67, respectively, suggesting that ROC curves are not sufficiently reliable. Dark gray: PSG-AHI 10/h; light gray: PSG-AHI 5/h.

Reliability of OCST at various 3% ODI cutoffs for PSG-AHI 5/h in children.

3% ODI cutoff value (/h)	Ac (%)	Se (%)	Sp (%)	PLR	NLR	PPV (%)	NPV (%)
10	61.5	**45.3**	81.1	2.402	**0.674**	74.4	**55.1**
15	59.8	31.3	94.3	5.521	0.729	87.0	53.2
20	54.7	20.3	96.2	5.383	0.828	86.7	50.0
25	53.0	15.6	**98.1**	**8.281**	0.860	**90.9**	49.1

What about nocturnal oximetry?



The answer my friends is blowing in the wind.....

Sleep Medicine Reviews 27 (2016) 96–105

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CLINICAL REVIEW

Pediatric OSAS: Oximetry can provide answers when polysomnography is not available

Athanasios Kaditis [a, *], Leila Kheirandish-Gozal [b], David Gozal [b]

Table 2
Studies evaluating clusters of desaturation events as predictor of obstructive sleep apnea syndrome defined by polysomnography.

Author, year	Type of study	Quality of evidence	Subjects-Methods	Definitions: OSAS by polysomnography and abnormal oximetry	Key findings
Brouillette et al., 2000 [12]	Cross-sectional study	IV	Nocturnal oximetry was analyzed in 349 children (6 mo-18 y) who underwent polysomnography for suspected OSAS (duration ≥6 h).	OSAS: mixed/obstructive AHI ≥1 episode/h Abnormal oximetry: three or more clusters of desaturations (≥3 desaturations ≥4% within 10–30 min) and ≥3 SpO_2 drops to <90%.	Abnormal oximetry had 97% positive predictive value for OSAS.
Nixon et al., 2004 [7]	Study in three phases	III	Phase 1-prospective: 64 children who underwent adenoidectomy and/or tonsillectomy had preoperative nocturnal oximetry. Phase 2-retrospective: 349 children who underwent adenoidectomy and/or tonsillectomy had preoperative polysomnography or cardiorespiratory sleep study and the oximetry recording was analyzed. Phase 3-prospective: 230 children (median age 4.3 y) who underwent adenoidectomy and/or tonsillectomy and had preoperative nocturnal oximetry (duration ≥6 h).	Phase 1: four categories of the McGill oximetry score were defined according to the presence of ≥3 clusters of desaturation events and three or more SpO_2 drops to <90%, <85% or <80% (normal/inconclusive oximetry, mildly, moderately or severely abnormal).	Phases 2 and 3: The McGill oximetry score correlated significantly with AHI and predicted the risk of postoperative respiratory complications.
Payone et al., 2013 [29]	Prospective, cohort study	III	148 otherwise healthy children (1.2–11.8 y) referred for suspected OSAS underwent two consecutive nocturnal oximetries at home (duration ≥6 h).	Abnormal oximetry: McGill oximetry score >1.	The night-to-night agreement for abnormal oximetry was 97%; the night-to-night agreement for McGill oximetry score was 89.9%.
Velasco Suárez et al., 2013 [30]	Prospective cohort study	III	167 otherwise healthy children (2–16 y) with adenotonsillar hypertrophy and suspected OSAS underwent polysomnography (mean duration 5 h); the pulse oximetry recording was analyzed.	OSAS: AHI >1 episode/h. Abnormal oximetry: at least two clusters of desaturation events and at least one SpO_2 drop below 90%.	Pulse oximetry had 86.6% sensitivity, 98.9% specificity, 98% positive predictive value and 90.1% negative predictive value for OSAS.
Coverstone et al., 2014 [31]	Retrospective cohort study	IV	114 children with Down syndrome (mean age 7 years; range 1.8 months–21.4 y) who underwent polysomnography for suspected obstructive SDB; a McGill oximetry score of 1–4 was calculated from the oximetry channel of polysomnography.	OSAS: obstructive AHI ≥2.5 episodes/h. Abnormal oximetry: McGill oximetry score of 3 or 4.	McGill oximetry score of 3 or 4 had specificity of 98% and positive predictive value of 94% for OSAS; McGill score >1 had specificity and positive predictive value of 71% for detecting OSAS; 10% of patients had central apnea index ≥2.5 episodes/h although their obstructive AHI was <2.5 episodes/h and 53.8% of them had McGill score of 2.
Lin et al., 2014 [28]	Case-control study	IV	49 children with Down syndrome matched for age, gender and OSAS severity with 49 typically developing children (46 females; mean age 6.2; range 0.3–16.9 y); participants underwent polysomnography.	OSAS: obstructive AHI >1 episode/h. Abnormal oximetry: McGill oximetry score >1.	When comparing children with Down syndrome and matched typically developing children, abnormal oximetry had essentially similar sensitivity (43% vs 37%), specificity (93% vs 93%), positive predictive value (94% vs 93%), and negative predictive value (39 vs 37%) for OSAS.

Abbreviations: AHI: apnea-hypopnea index, OSAS: obstructive sleep apnea syndrome, SDB: sleep-disordered breathing, SpO_2: oxygen saturation of hemoglobin.

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CLINICAL REVIEW

Pediatric OSAS: Oximetry can provide answers when polysomnography is not available

Athanasios Kaditis [a, *], Leila Kheirandish-Gozal [b], David Gozal [b]

Table 3
Studies evaluating the oxygen desaturation index as predictor of obstructive sleep apnea syndrome defined by polysomnography.

Author, year	Type of study	Quality of evidence	Subjects-Methods	Definitions: OSAS by polysomnography and abnormal oximetry	Key findings
Brouillette et al., *2000* [12]	Cross-sectional study	IV	Nocturnal oximetry was analyzed in 349 children (6 mo-18 y) who underwent polysomnography for suspected OSAS.		ODI_4 had high correlation with the mixed/obstructive AHI ($r^2 = 0.78$; $P < 0.001$).
Kirk et al., *2003* [36]	Prospective cohort study	IV	58 otherwise healthy children (4–18 y) referred for suspected OSAS; oximetry was performed for two nights at home; also oximetry and polysomnography in the hospital; an automated oximetry analysis algorithm was used.	OSAS: AHI ≥1 episode/h. Moderate OSAS: AHI >5 episodes/h. Abnormal oximetry: ODI_4 >5 episodes/h.	ODI_4 had high test-retest reliability; agreement between ODI_4 and AHI was poor especially for AHI >10 episodes/h (underestimation of AHI); abnormal ODI_4 had 66.7% sensitivity and 60% specificity for moderate OSAS.
Chang et al., *2013* [34]	Retrospective, cohort study	III	141 children (21 m.o.-12.8 y) who underwent polysomnography for suspected OSAS; symptom questionnaire (presence of mouth breathing: score = 1; restless sleep: score = 1) and ODI_4 (≤1 episode/h: score = 0; >1 and ≤ 3 episodes/h: score = 1; >3 episodes/h: score 2) were used to calculate a total score.	OSAS: AHI >5 episodes/h. Abnormal oximetry: ODI_4 >1 episode/h.	Abnormal oximetry had 78% sensitivity, 57% specificity and 69% positive predictive value for OSAS; a total score ≥3 had 60% sensitivity, 86% specificity and 84% positive predictive value for OSAS.
Tsai et al., *2013* [35]	Retrospective cohort study	IV	148 otherwise healthy children (3–12 y) referred for suspected OSAS underwent polysomnography.	OSAS: AHI ≥1 episode/h. Abnormal oximetry: ODI_4 >2.05 episodes/h.	Abnormal oximetry had 77.7% sensitivity, 88.9% specificity and 98.1% positive predictive value.
Stores et al., *2014* [33]	Cross-sectional study	IV	31 children with Down syndrome (mean age 8.7; range 2.3–16.3 y); 20 children underwent nocturnal oximetry at home.	Abnormal oximetry: desaturation (>4%) index >1.4 episodes/h.	25% of children had abnormal oximetry (SDB).

Nocturnal Pulse Oximetry as an Abbreviated Testing Modality for Pediatric Obstructive Sleep Apnea

Pediatrics 2000;105

Robert T. Brouillette, MD*; Angela Morielli, MBA, RPSGT*; Andra Leimanis, BSc*
Karen A. Waters, MBBS, PhD‡; Rina Luciano, RRT*; and Francine M. Ducharme, MD*

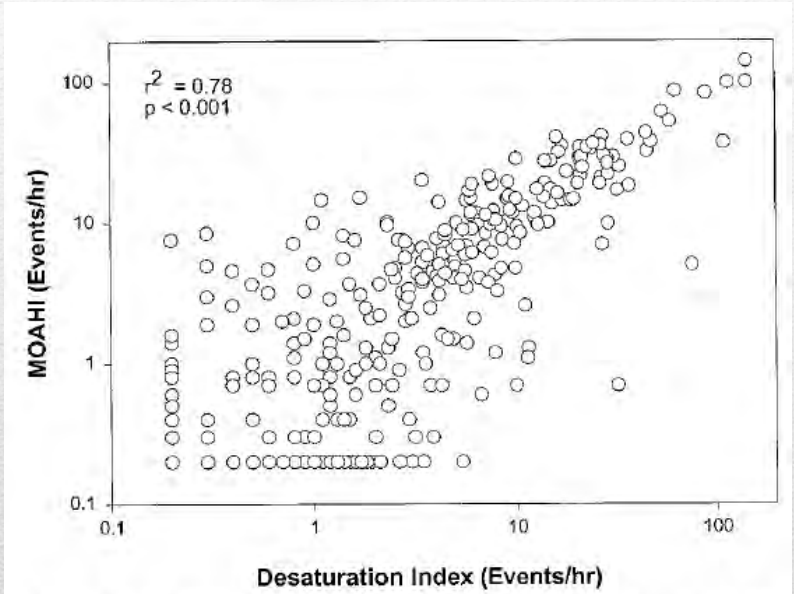
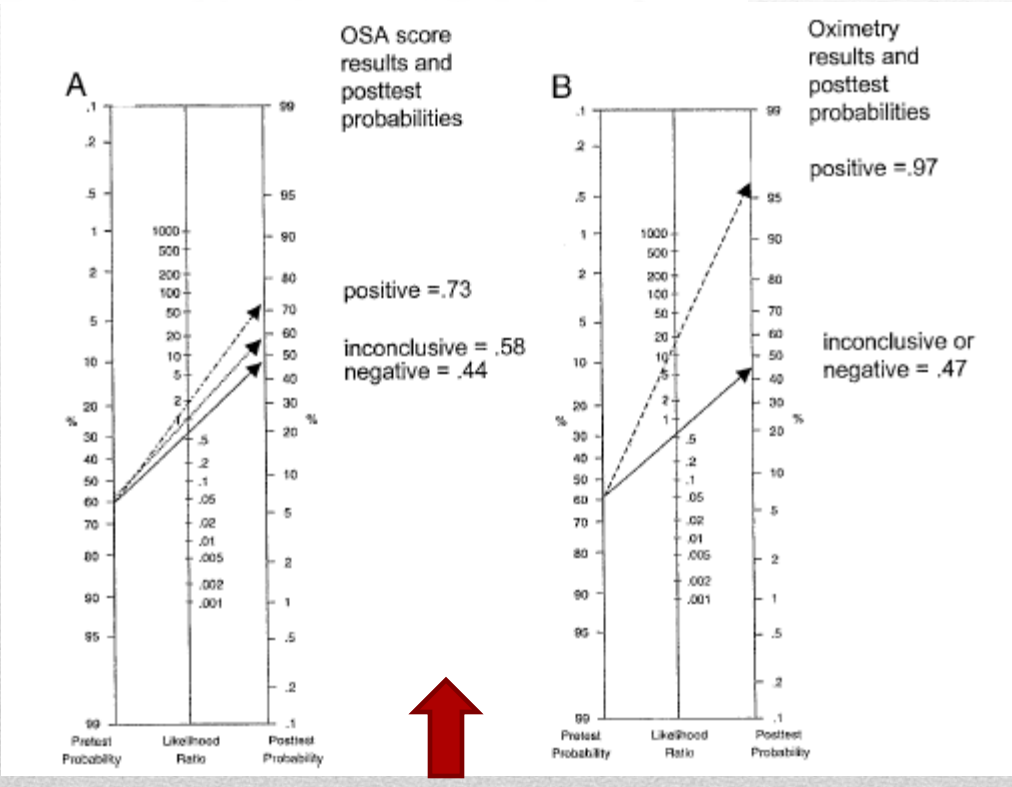


Fig 2. This figure shows the MOAHI versus the desaturation index for 349 children referred for possible obstructive apnea. The MOAHI and the desaturation index were highly correlated. However, some patients had repetitive desaturations without apnea and others had repetitive apneas without desaturation.



A, this nomogram shows the pretest probability (60%), likelihood ratios, and posttest probabilities for OSA scores predicting OSA (positive), inconclusive, or predicting no OSA (negative).

B, this nomogram shows the pretest probability (60%), likelihood ratios and posttest probabilities for pulse oximetries interpreted as positive and for those read as inconclusive/negative.

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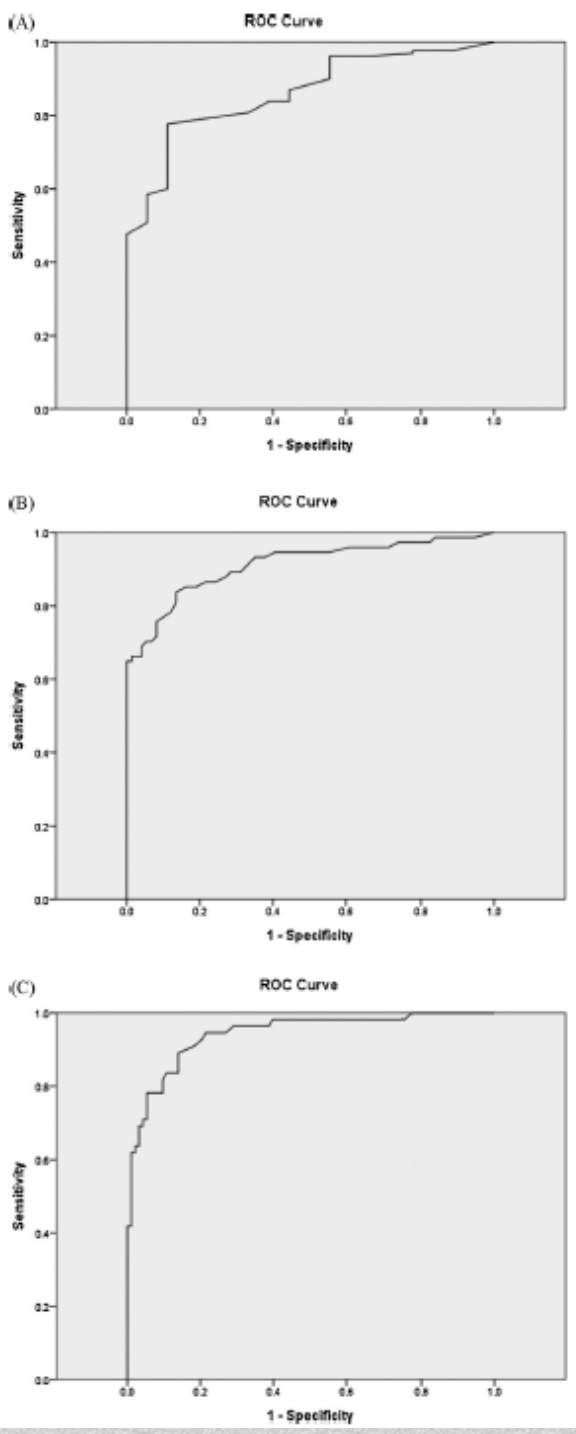
Usefulness of desaturation index for the assessment of obstructive sleep apnea syndrome in children

Chih-Min Tsai [a], Chia-Hao Kang [a], Mao-Chang Su [b], Hsin-Ching Lin [c], Eng-Yen Huang [d], Chih-Cheng Chen [a], Jui-Chieh Hung [e], Chen-Kuang Niu [a], Da-Ling Liao [b], Hong-Ren Yu [a,*]



ROC curve of desaturation index (DI) for the prediction of (A) mild, (B) moderate and (C) severe OSAS.

(A) For mild OSAS prediction, the best cutoff value of DI was 2.05 (sensitivity 77.7%; specificity 88.9%). The area under ROC curve is 0.859.

(B) For moderate OSAS prediction, the best cutoff value of DI is 3.50 (sensitivity 83.8%; specificity 86.5%). The area under ROC curve is 0.911.

(C) For severe OSAS prediction, the best cutoff value of DI predicting severe OSAS is 4.15 (sensitivity 89.1%; specificity 86.0%). The area under ROC curve is 0.942.

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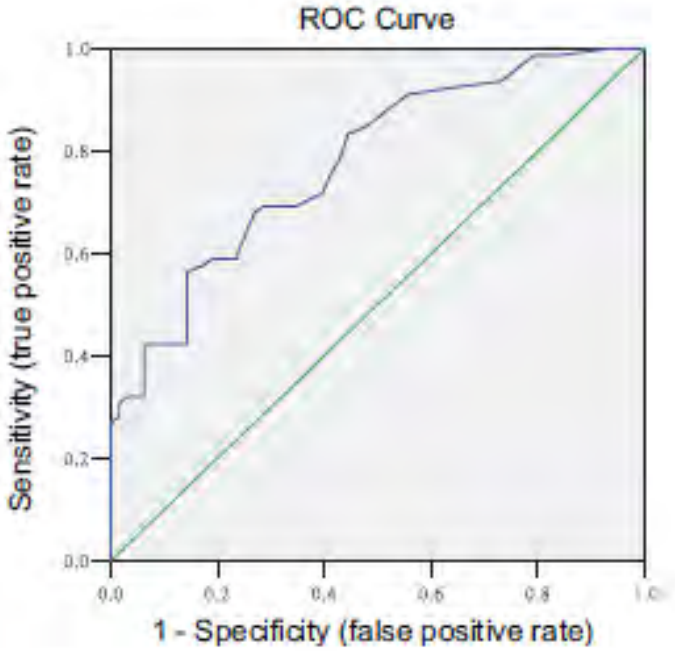
Combination of symptoms and oxygen desaturation index in predicting childhood obstructive sleep apnea

Li Chang [a], Jianxin Wu [b], Ling Cao [a,*]



Diagnostic predictive values of symptoms and ODI for OSA in children.

Variable	Sensitivity	Specificity	PLR	NLR	PPV	NPV
Mouth breathing	0.86	0.29	1.20	0.49	0.60	0.62
Restless sleep	0.69	0.48	1.32	0.65	0.62	0.56
Observable apnea during sleep	0.21	0.95	4.31	0.83	0.84	0.49
ODI = 1	0.78	0.57	1.82	0.38	0.69	0.68

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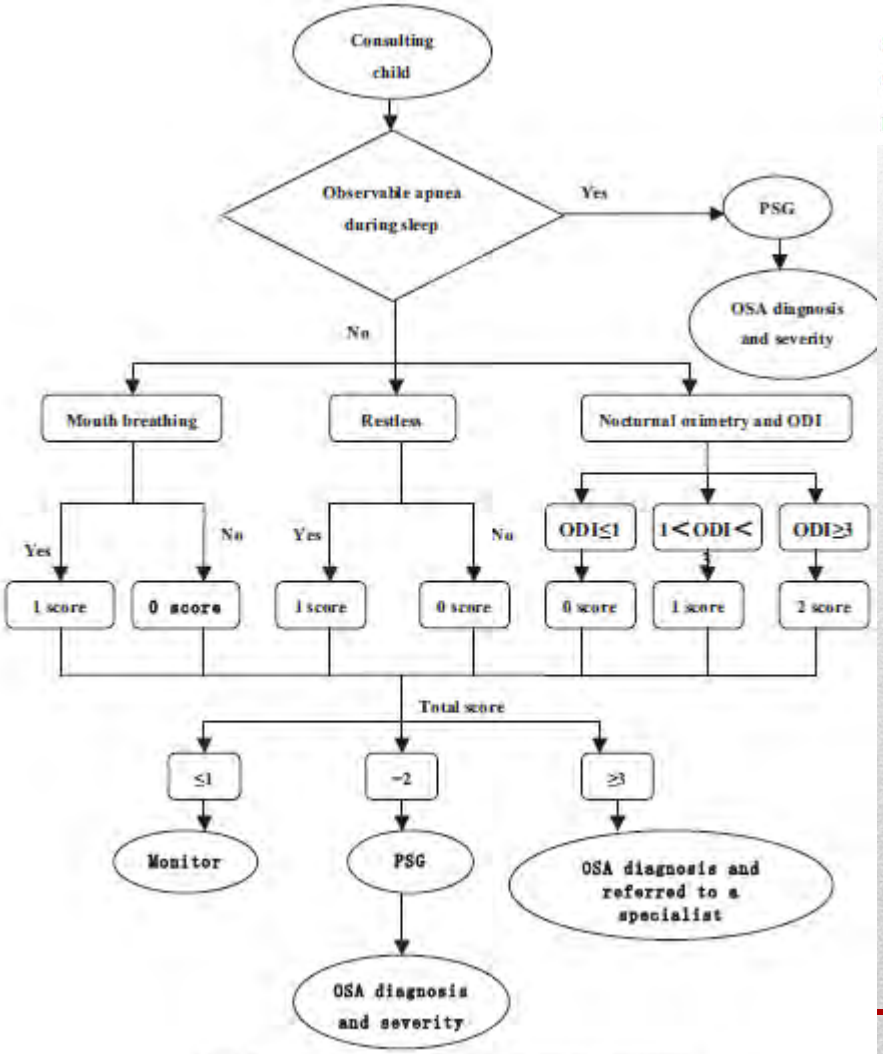

Graph 3. Screening process based on symptoms and ODI for OSA in children.

Diagnostic predictive value of association of symptoms and ODI for OSA in children.

Total score	Sensitivity	Specificity	PLR	NLR	PPV	NPV
≥2	0.92	0.38	1.49	0.2	0.65	0.80
≥3	0.60	0.86	4.22	0.46	0.84	0.64

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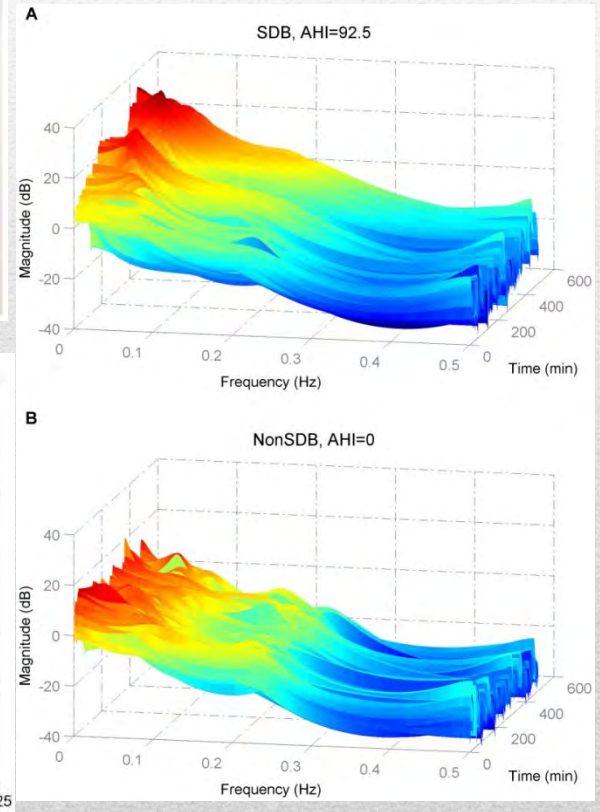
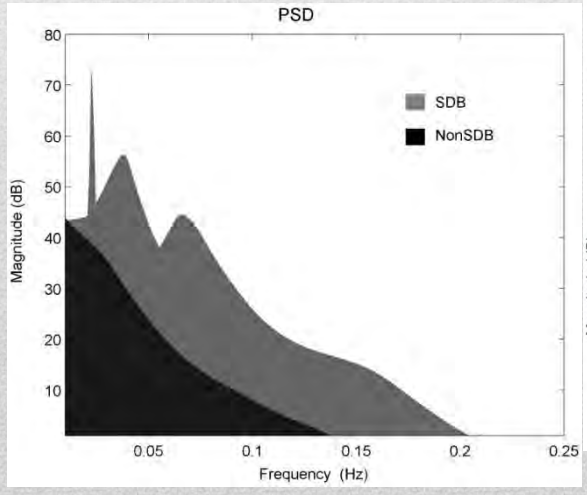
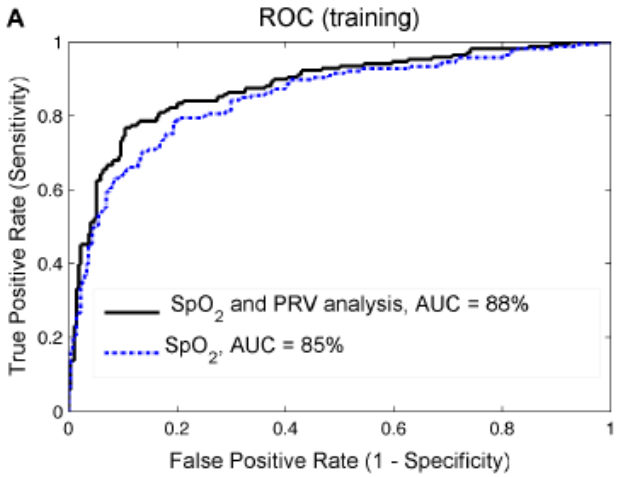
PLOS ONE

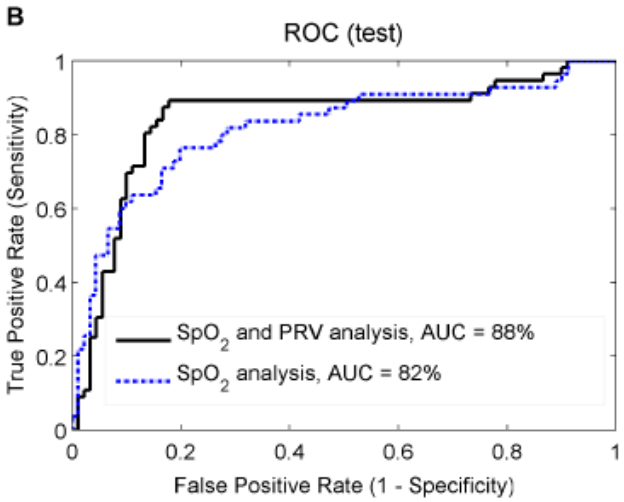
Development of a Screening Tool for Sleep Disordered Breathing in Children Using the Phone Oximeter™

Ainara Garde[1]*, Parastoo Dehkordi[1], Walter Karlen[1], David Wensley[3], J. Mark Ansermino[1,2], Guy A. Dumont[1]









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Editorial

Diagnóstico del síndrome de apnea hipopnea del sueño en niños: pasado, presente y futuro

Diagnosing Sleep Apnea-Hypopnea Syndrome in Children: Past, Present, and Future

Pablo E. Brockmann [a], María Luz Alonso-Álvarez [b] y David Gozal [c,*]

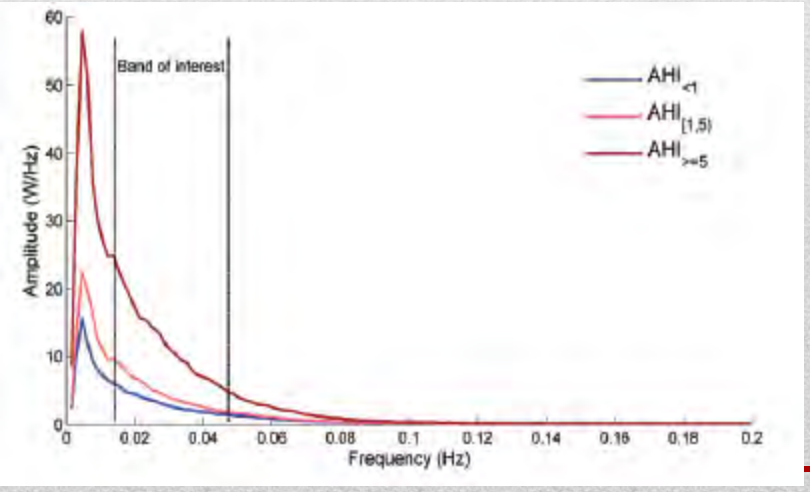
Analysis and Classification of Oximetry Recordings to Predict Obstructive Sleep Apnea Severity in Children

Gonzalo C. Gutiérrez-Tobal, *Student Member, IEEE*, Leila Kheirandish-Gozal, Daniel Álvarez, *Member, IEEE*, Andrea Crespo, Mona F. Philby, Meelad Mohammadi, Félix del Campo, David Gozal, and Roberto Hornero, *Senior Member, IEEE*

TABLE I. DEMOGRAPHIC AND CLINICAL DATA

	All	$AHI_{<1}$	$AHI_{[1,5)}$	$AHI_{\geq 5}$
# Subjects	176	30	75	71
Age* (years)	7.0±3.6	8.2±3.3	7.3±3.5	6.1±3.6
Male (%)	55.1	56.7	54.7	54.9
BMI* (kg/m^2)	20.6±7.3	20.5±6.8	20.6±6.7	20.7±8.2
AHI (e/h)	-	0.5±0.3	2.6±1.1	19.3±23.1

BMI: Body Mass Index; AHI: Apnea Hypopnea Index; *p-value=0.016; *p-value=0.816



Feature extraction. SpO_2 recordings were parameterized computing 17 features: i) time domain statistics, first-to-fourth statistical moments (*M1t-M4t*); ii) frequency domain statistics, *M1f-M4f*, median frequency (MF), spectral entropy (SE); iii) conventional spectral features, total power (PT), peak amplitude (PA), relative power (PR); iv) nonlinear measures, sample entropy (SampEn), central tendency measure (CTM), Lempel-Ziv complexity (LZC); and v) conventional oximetric indices, oxygen desaturation index (ODI3).

Feature selection. Fast correlation-based filter (FCBF) was applied to select relevant and non-redundant variables based on symmetric uncertainty (SU), which is a normalization of information gain (IG).

Feature classification. Statistical pattern recognition techniques were used for binary classification:

Linear discriminant analysis (LDA)

Quadratic discriminant analysis (QDA)

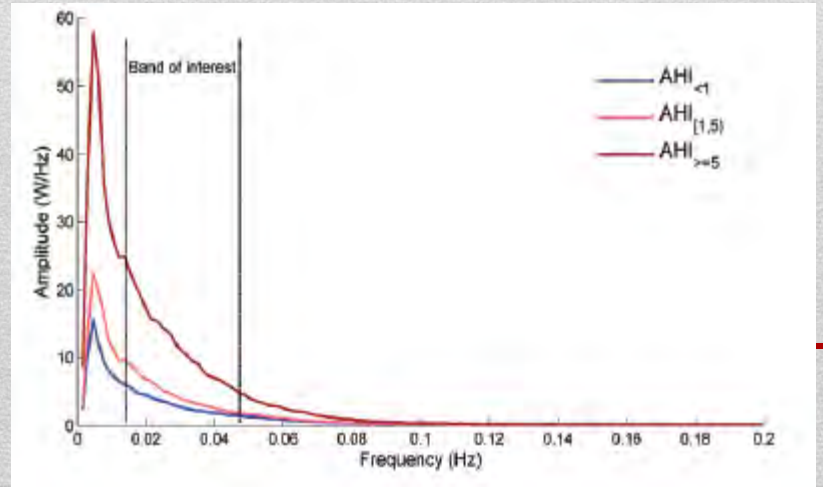
Logistic regression (LR)

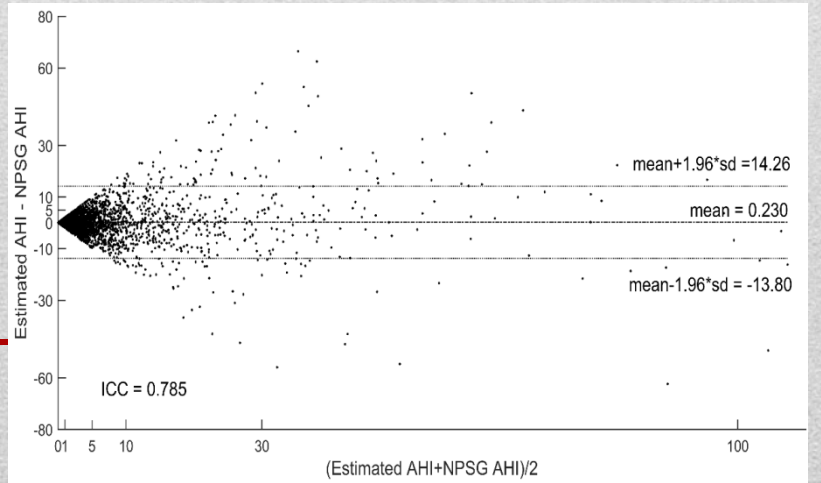
TABLE IV. DIAGNOSTIC ABILITY OF MLP AND ODI_3 (BINARY CLASSIFICATION AFTER LOO-CV)

	Se (%)	Sp (%)	Acc (%)	*PPV* (%)	*NPV* (%)	*LR+*	*LR-*
ODI_3 (AHI=1)	78.1	80.0	78.4	95.0	48.9	3.91	0.27
ODI_3 (AHI=5)	69.0	81.9	76.7	79.6	72.1	3.81	0.38
MLP (AHI=1)	91.8	50.0	**84.7**	89.9	55.6	1.84	0.16
MLP (AHI=5)	70.4	96.2	**85.8**	92.6	82.8	18.5	0.31

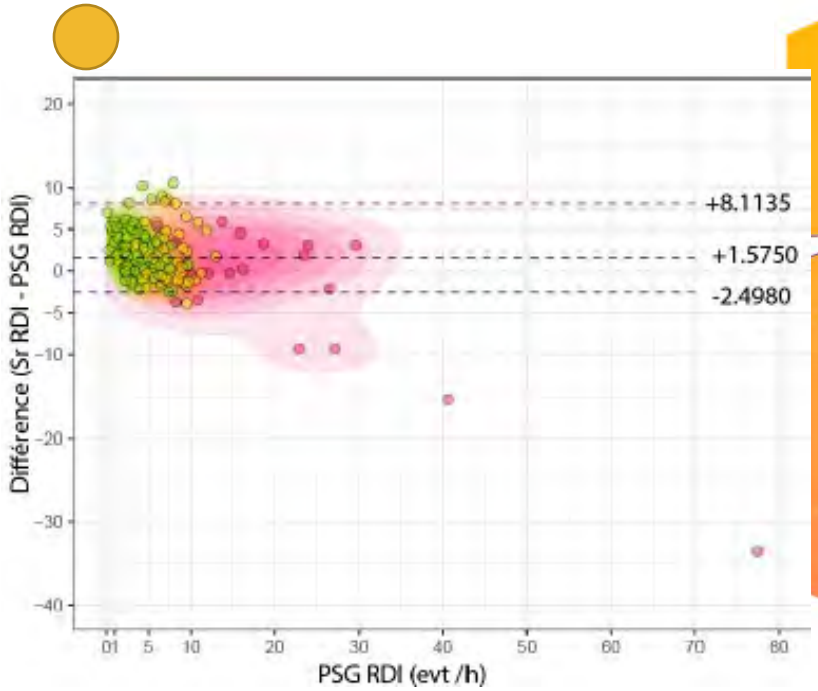
Machine Classification and AI-Based Neural Network Approaches to Automated Nocturnal Oximetry Diagnostics

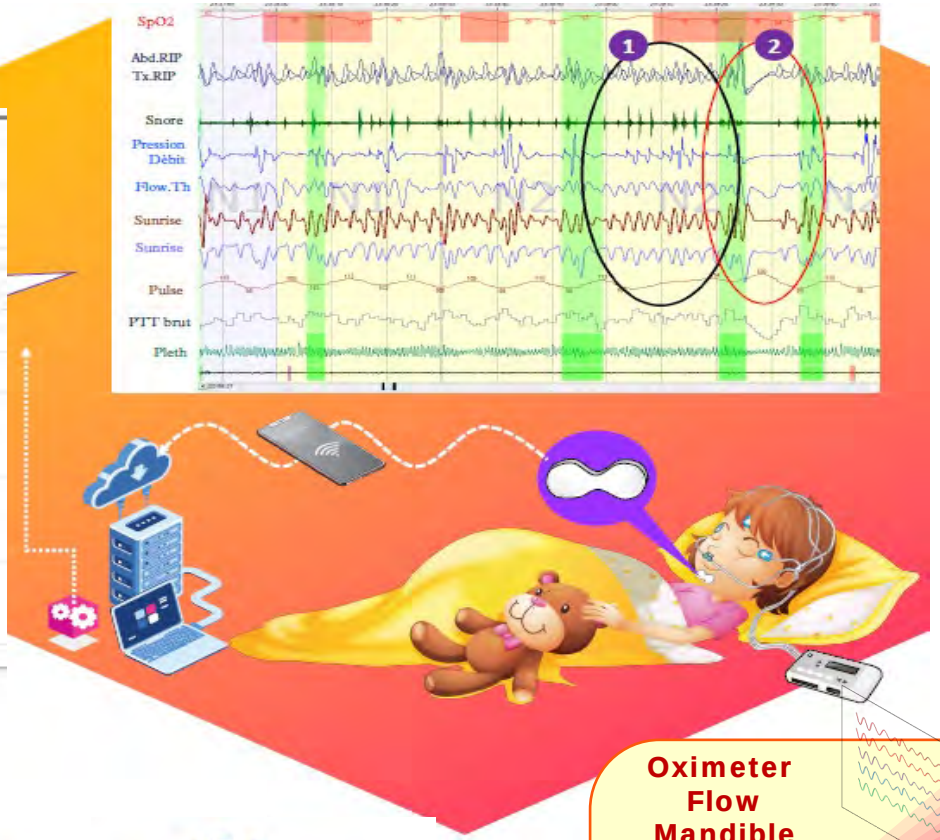
Center	Participants	Age	Male (%)	BMI (kg/m²)	AHÍ (/hrTST)	OSA for AHI = 1 e/h (%)	OSA for AHI = 5 e/h (%)	OSA for AHI = 10 e/h (%)
UofC[1]	981	6.1 ± 3.4	61.4	19.7 ± 7.3	9.3 ± 17.2	82.2	41.3	23.3
UofTn[2]	611	11.5 ± 21.4	54.6	23.3 ± 10.1	5.8 ± 11.3	68.1	29.6	17.7
HUBU[3]	578	4.1 ± 2.2	61.8	17.1 ± 4.2	5.9 ± 11.3	64.5	26.3	15.2
BCH[4]	558	6.3 ± 5.3	66.3	17.8 ± 3.7	5.8 ± 11.7	65.1	27.4	17.0
MSU[5]	499	6.5 ± 5.0	55.5	17.8 ± 11.2	6.2 ± 9.3	85.8	22.0	14.8
CGMH[6]	283	9.9 ± 3.2	72.4	19.5 ± 4.6	4.3 ± 10.0	72.4	21.9	8.1
Uof HK[7]	202	10.0 ± 2.4	62.9	18.7 ± 4.6	4.9 ± 7.5	70.3	26.2	10.4
PUCC[8]	183	5.4 ± 4.8	52.5	17.8 ± 4.2	3.7 ± 9.1	60.1	18.6	7.6
UofA[9]	130	11.7 ± 3.1	37.7	30.3 ± 5.7*	3.2 ± 7.1	63.1	22.3	10.0
SJDCH[10]	60	8.4 ± 4.8	58.3	19.5 ± 5.2	4.2 ± 6.1	76.7	25.0	11.6
ASCH[11]	51	7.0 ± 3.4	66.7	20.6 ± 6.4	10.6 ± 13.8	90.2	54.9	37.2
UofTu[12]	36	10.4 ± 3.5	61.1	21.0 ± 8.0	6.9 ± 12.9	72.2	27.8	16.7
HSM[13]	19	6.5 ± 3.8	47.4	19.1 ± 6.8	11.0 ± 15.2	73.7	47.4	36.8
ALL	**4,191**	**7.4 ± 9.3**	**60.0**	**20.0 ± 7.0**	**6.4 ± 12.5**	**72.9**	**29.6**	**16.8**





Hornero et al, AJRCCM 2017





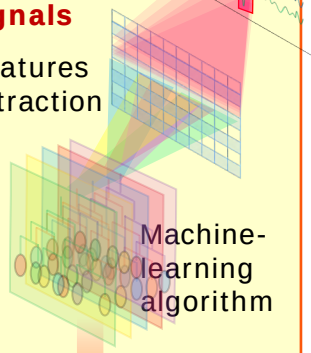
Sleep data collection

Cloud storage

Machine learning algorithm

Oximeter
Flow
Mandible
signals

Features extraction



Machine-learning algorithm

Estimated AHI and ODI3% from oximetry measurements

AI-based Machine Learning Algorithm for Automatic Diagnosis of OSA Using Overnight Home-Based (Pick your favorite sensor(s)):

ORIGINAL ARTICLE: SLEEP & BREATHING

WILEY

Clinical validation of a mandibular movement signal based system for the diagnosis of pediatric sleep apnea

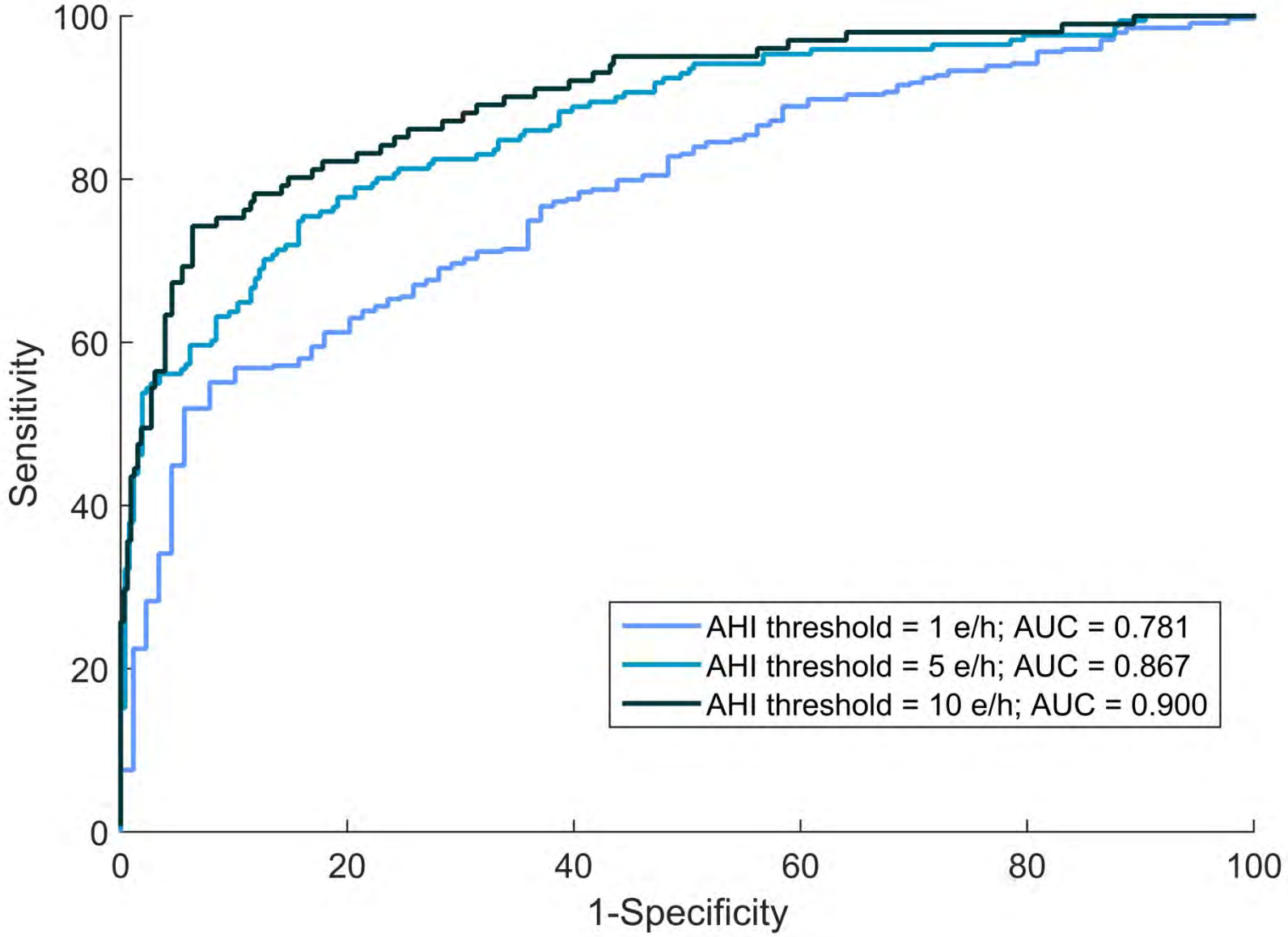
Jean-Benoit Martinot MD[1,2] | Valérie Cuthbert MSc[1] | Nhat N. Le-Dong PhD[3] | Nathalie Coumans MSc[1] | Deborah De Marneffe MSc[1] | Clément Letesson PhD[3] | Jean L. Pépin MD, PhD[4] | David Gozal MD, MBA[5,6]

Easy communication between patients and physicians

Cloud Algorithm-Driven Oximetry-Based Diagnosis of Obstructive Sleep Apnea in Symptomatic Habitually-Snoring Children. Xu et al, *ERJ* 2019

	All Participants (n=432)	Primary Snoring $AHI_{PSG} \leq 1$ event/hr (n = 89)	OSAS $AHI_{PSG} > 1$ event/hr (n = 343)	OSAS $AHI_{PSG} > 5$ events/hr (n = 171)	p value
Age, years	6.3 ± 2.5	6.5 ± 2.4	6.3 ± 2.6	6.4 ± 2.5	
Male, %	65.3 %	62.8%	69.4 %	64.5 %	
BMI (% obese)	17.8 ± 4.5 (26.3)	16.6 ± 3.9 (23.2)	18.3 ± 4.7 (26.7)	19.2 ± 5.4 (33.1%)*	*-p<0.01 vs. all other
Total Sleep Time (min)	474.1± 54.4	460.4± 72.2	478.1± 47.8	471.7± 48.4	
Sleep efficiency (%)	83.5 ± 8.6	83.7 ± 8.9	83.5 ± 8.6	82.2 ± 8.8	
AHI, events/ h (median; IQR)	10.0 ± 21.3 (3; 8.1))	0.5 ± 0.3 (0.5; 0.5)	11.4 ± 23.3 (4.5, 9.6)	22.3 ± 29.6 (12.2; 16.4)	**p<0.0001 vs. primary snoring
ODI3%, events/ h	6.7 ± 16.2	0.2 ± 0.7	8.3 ± 17.7	14.8 ± 21.4	** p<0.0001 vs. primary snoring
SpO_2 nadir, (range)	89.8 ± 7.2	94.3 ± 2.0	88.6 ± 7.6	85.2 ± 9.0	** p<0.0001 vs. primary snoring

Xu et al, *ERJ* 2019



ALGORITHM FOR THE DIAGNOSIS AND TREATMENT OF PEDIATRIC OSA

Step 1. Child is at risk for OSA (one or more):

- Parents report symptoms of OSA
- Physician identifies symptoms of OSA using structured questionnaire
- Conditions predisposing to OSA are present (adenotonsillar hypertrophy-allergic rhinitis, obesity, craniofacial abnormalities, neuromuscular disorders)
- History of prematurity
- Family history of OSA

Step 2a. OSA-related morbidity is recognized (one or more):

- Systolic or diastolic blood pressure >95th percentile for gender, age and height, or pulmonary hypertension
- Daytime sleepiness, hyperactivity, inattention, academic difficulties
- Inadequate somatic growth
- Enuresis

Step 2b. Conditions frequently coexisting with OSA are identified (one or more):

- Recurrent otitis media, tympanostomy tubes
- Recurrent wheezing
- Oral-motor dysfunction
- Metabolic syndrome

Step 3. Factors predicting OSA persistence are present (at least one):

- Male gender
- Increasing Body Mass Index percentile, development of obesity

Step 4. Objective evaluation for OSA severity:

- Overnight polysomnography
- If not available: nocturnal pulse oximetry

Step 5. Child is a potential candidate for treatment if at risk for OSA (step 1) and at least one criterion:

- AHI >5 episodes/h
- AHI 1-5 and OSA morbidity present (step 2a)
- AHI 1-5 and risk factor for OSA persistence (step 3)
- AHI 1-5 and neuromuscular disorder or craniofacial abnormalities present (step 1)
- ≥3 SpO_2 drops <90% and ≥3 clusters of desaturation events or alternatively, desaturation (≥3%) index ≥3.5 episodes/h

Or if polysomnography or oximetry not available:

- Frequently or almost always loud snoring and male gender
- Frequently or almost always loud snoring and sleepiness
- Frequently or almost always loud snoring and learning problems

Priority for treatment increases if coexisting OSA-related conditions are present that may also improve with treatment (step 2b)

Step 6. Stepwise treatment approach:

1. Weight control for obesity
2. Trial of nasal corticosteroids for adenoidal hypertrophy prior to adenoidectomy
3. Adenotonsillectomy for adenotonsillar hypertrophy
4. Orthodontic devices for mandibular malpositioning, narrow maxilla
5. nCPAP for: i) residual OSA after adenotonsillectomy; ii) OSA related to obesity, neuromuscular disorders or craniofacial abnormalities and unresponsive to other measures
6. Craniofacial surgery or tracheostomy if other treatment modalities fail

Notes

1. Information collected in steps 1-4 is used to identify children requiring treatment for OSA (step 5) and to determine the appropriate therapeutic modalities (step 6). Please refer to the text for details.
2. Step 6 represents a hierarchical approach to OSA treatment.

Sleep Medicine 13 (2012) 217–227

Contents lists available at SciVerse ScienceDirect

Sleep Medicine

journal homepage: www.elsevier.com/locate/sleep

Review Article

Algorithm for the diagnosis and treatment of pediatric OSA: A proposal of two pediatric sleep centers

Athanasios Kaditis [a,*], Leila Kheirandish-Gozal [b], David Gozal [b]

[a] Pediatric Pulmonology Unit, Sleep Disorders Laboratory, First University Department of Pediatrics, University of Athens School of Medicine and Aghia Sophia Children's Hospital, Athens, Greece
[b] Section of Pediatric Sleep Medicine, Department of Pediatrics, Pritzker School of Medicine, The University of Chicago, Chicago, IL, USA

So, how do we go about diagnosing OSA?

Adapt, Adapt, Adapt!!!

Clinical diagnosis of OSA: Still Stuck with PSG

Polysomnography

- Gold-standard method
- Expensive
- Labor intensive
- Interpretation by expert
- Very limited throughput

At home sleep tests

- E.g. Multichannel
- ‘Less expensive’
- Less accurate
- Limited throughput

OSA associates with numerous co-morbidities

- Molecular/Cellular abnormalities
  - Inflammation
  - Oxidative stress
  - Endothelial dysfunction
  - Immune cell modulation
  - Neurological dysfunction

- End-Organ Adverse Consequences
  - Neurocognitive abnormalities
  - Dyslipidemia
  - Hypertension and Atherosclerosis
  - Insulin Resistance
  - Depression
  - Enuresis

Biomarker Discovery Phases

Five phases have been proposed by the National Institutes of Health (NIH) 'Early Detection Research Network' in the process of evaluating biomarkers:

- Phase I includes exploratory studies in which biomarkers are discovered through knowledge-
- based profiling (genes or proteins) to distinguish between diseased and normal samples.
- Phase II has two important components, namely development of an assay and validation for reproducibility and portability to other laboratories.
- Phase III, the sensitivity and specificity of the test are appraised in a cohort of individuals who have not yet been diagnosed, a time consuming and usually onerous process, as blinded phenotyping of the cohort is needed in order to properly evaluate the biomarker panel.
- Phase IV should then evaluate the sensitivity and specificity of the test in a prospective cohort, in order to ascertain the false referral rate for treatment based on the tested biomarkers.
- Phase V evaluates the overall benefits and risks of the new diagnostic test on the screened population.

- In general, an ideal set of biomarkers should be safe, easy, inexpensive to measure, should track the success or failure of therapy, and should be consistent across sexes and ethnic groups. Furthermore, it should be sensitive and specific and have a high predictive value, which can be assessed using the diagnostic odds ratio (DOR)

DOR=(sensitivity/1-specificity)/(1-sensitivity/specificity) as well as by negative and positive likelihood ratios.

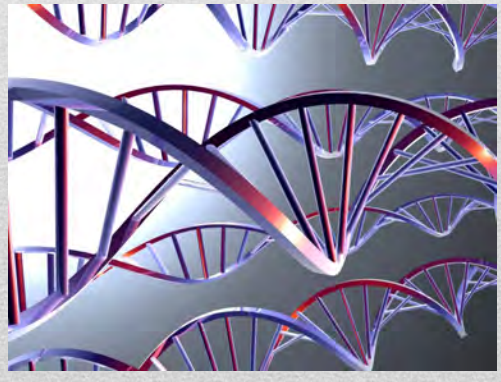
Evaluation of biomarkers and surrogate endpoints in chronic disease. In: Micheel CM, Ball JR, eds.; Committee on Qualifications of Biomarkers and Surrogate Endpoints in Chronic Disease; Institute of Medicine, The National Academies Press, 2010.

Clinical diagnosis of OSA:

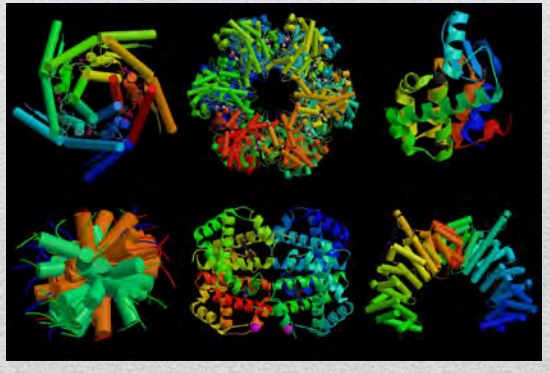
Biochemical testing (surrogate biomarkers)

- Simple and inexpensive
- High throughput
- *May serve as a rapid initial screening tool to select candidates for subsequent PSG analysis*
- Requires development and validation:

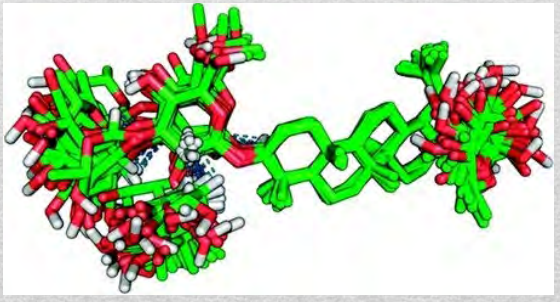
Transcriptional profiling & Epigenetics



Proteomics



Metabolomics



Problem

- Some children not fulfilling NPSG statistical criteria for "disease" may be symptomatic and display measurable morbidity

  while

- Other children who fulfill NPSG criteria for "disease" may not exhibit end-organ morbidity

Example: Rheumatic Fever

- The following Duckett Jones criteria are applied stringently for the diagnosis of ARF:
- Major criteria
  - Carditis
  - Polyarthritis
  - Chorea
  - Erythema marginatum
  - Subcutaneous nodules
- Minor criteria
  - Arthralgia
  - Fever
  - Elevated ESR or CRP
  - Prolonged PR interval
  - Evidence of preceding group A streptococcal infection–like from positive results on throat cultures or rapid antigen test
  - Elevated or rising streptococcal antibody titer

- If supported by evidence of preceding group A streptococcal infection, the presence of 2 major manifestations or 1 major and 2 minor manifestations indicates a high probability of ARF.
- Failure to fulfill the Jones criteria should make the diagnosis doubtful, except in situations in which rheumatic fever is first discovered after a long latent period, eg, Sydenham chorea or indolent carditis.

Tentative OSA Criteria:

Major	Minor
Obstructive apnea and hypopnea index >2 events/hour of sleep (/hrTST)	CRP > 0.4 μg/ml
Respiratory arousal index > 2/hrTST	HDL < 40 mg/dl
Nadir SpO2 < 90%	LDL > 80 mg/dl
Excessive Daytime Sleepiness	Fasting insulin > 20 μIU/ml
	Elevated norepinephrine/creatinine ratio (>85th percentile)
Academic Difficulties	Recurrent otitis media and/or s/p tympanostomy tubes
Hyperactive Behaviors	> 5 visits to Primary Care Physician/year for respiratory symptoms
Arterial Blood Pressure > 85th percentile	Adenoids ≥ +1
Enuresis	Tonsils ≥ +1
Obesity (BMI z score>1.67)	Asthma and/or allergic rhinitis
Adenoids ≥+2 and/or tonsils ≥+2	Family history of OSAS
	Nadir SpO2 >90% but < 93% *

If supported by a history of habitual snoring, we could propose the use of any 5 major criteria or of any 3 major and any 3 minor criteria as potentially and reliably indicating the presence of OSA that requires referral for treatment.

Gozal and Kheirandish-Gozal, Curr Opin Ped, 2008; Sleep Medicine 2010

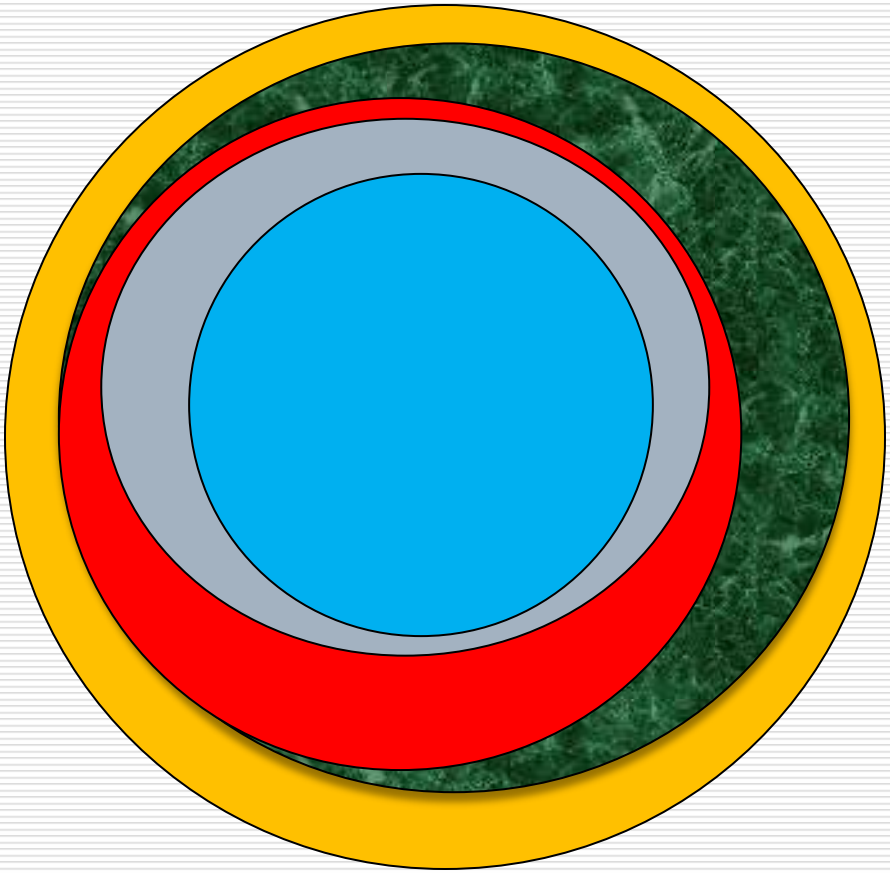
>7,000 **clinically referred** children with habitual snoring and symptoms of OSA

PSG shows oAHI>1 e/hTST

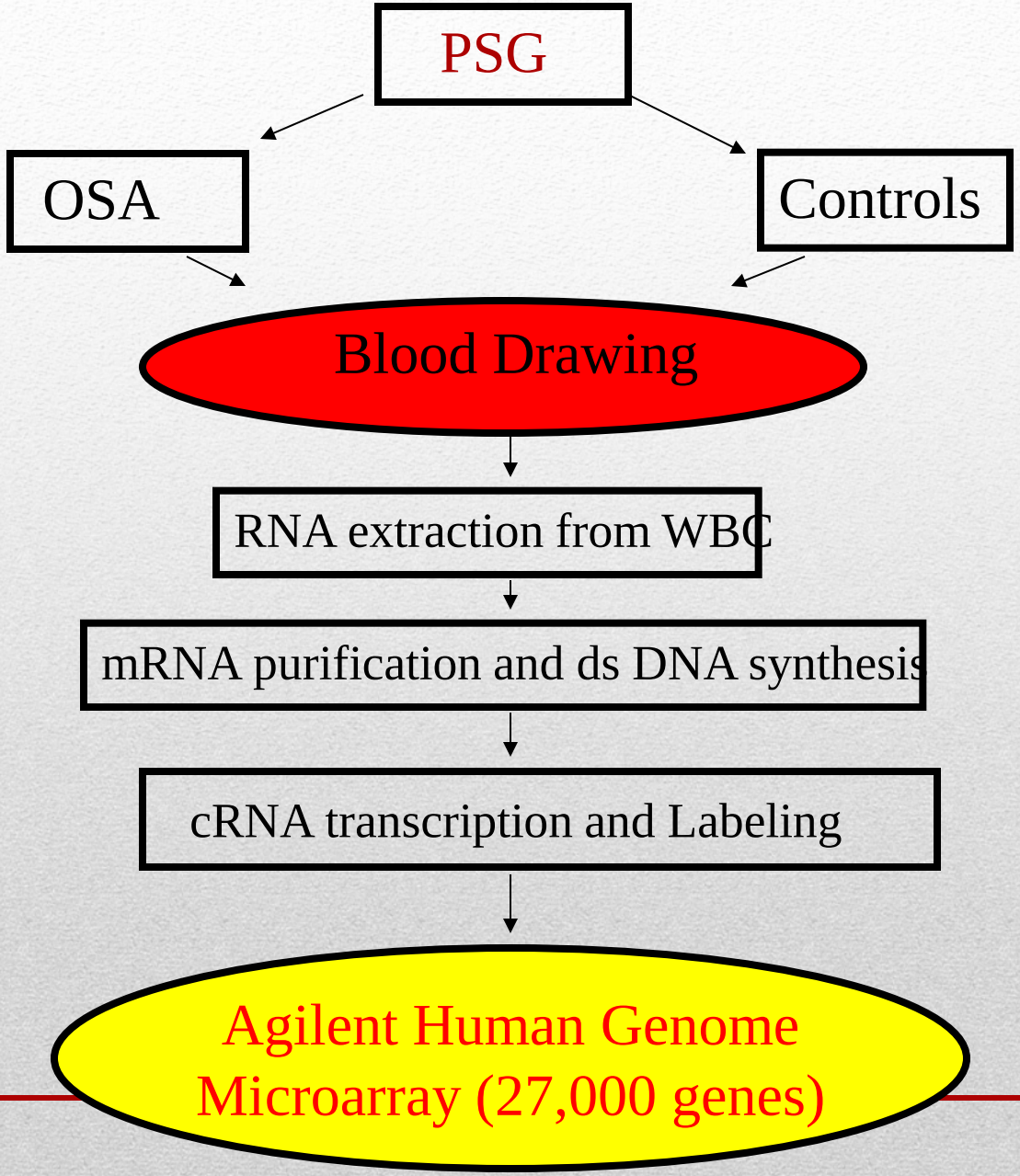
oAHI>2 e/hTST

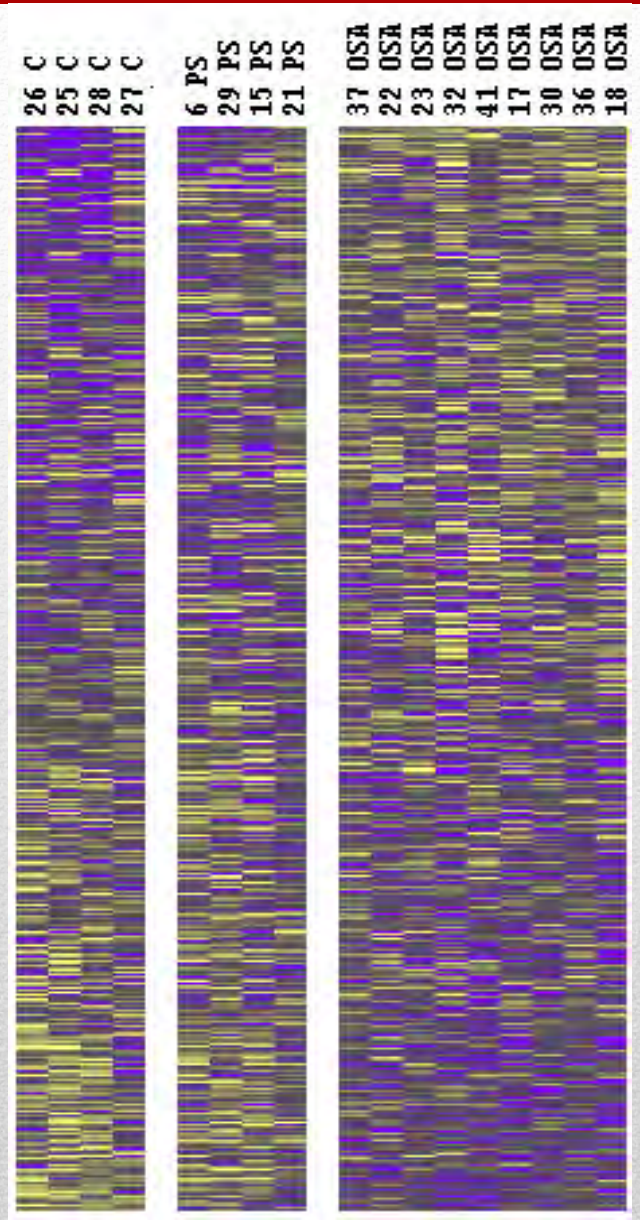
oAHI>5 e/hTST

When Gozal criteria are applied



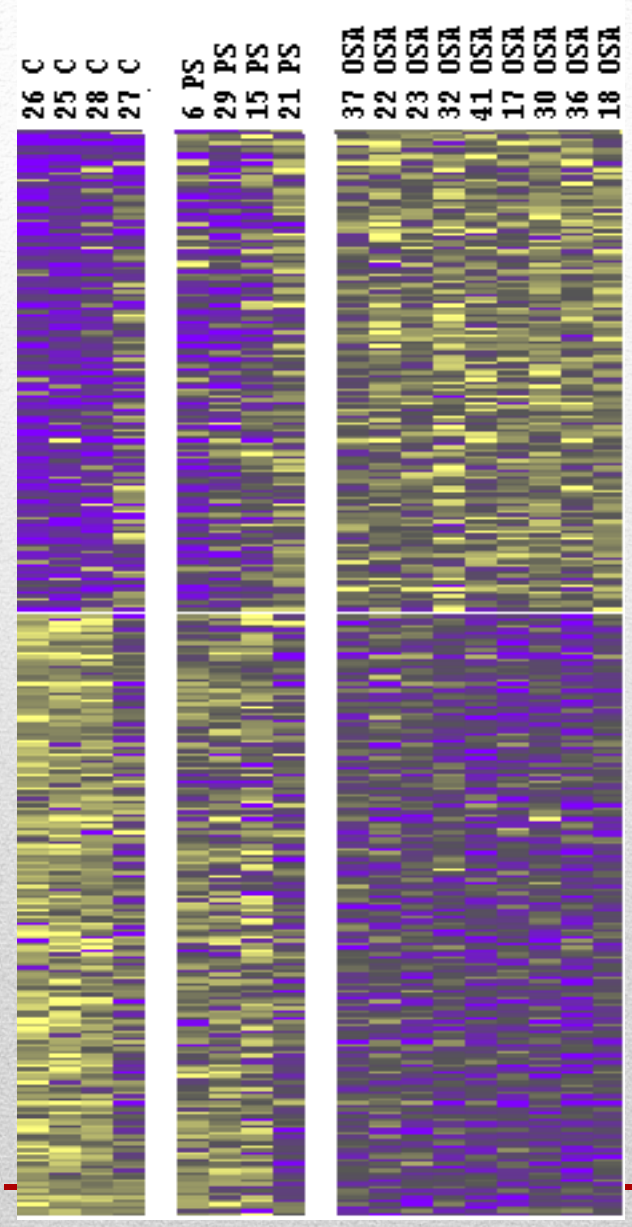
Blood Biomarkers


PSG
OSA
Controls
Blood Drawing
RNA extraction from WBC
mRNA purification and ds DNA synthesis
cRNA transcription and Labeling
Agilent Human Genome
Microarray (27,000 genes)



Infogram of gene expression pattern between each group.
Increased expression: brighter yellow
Decreased expression: darker blue

All genes that passed quality control



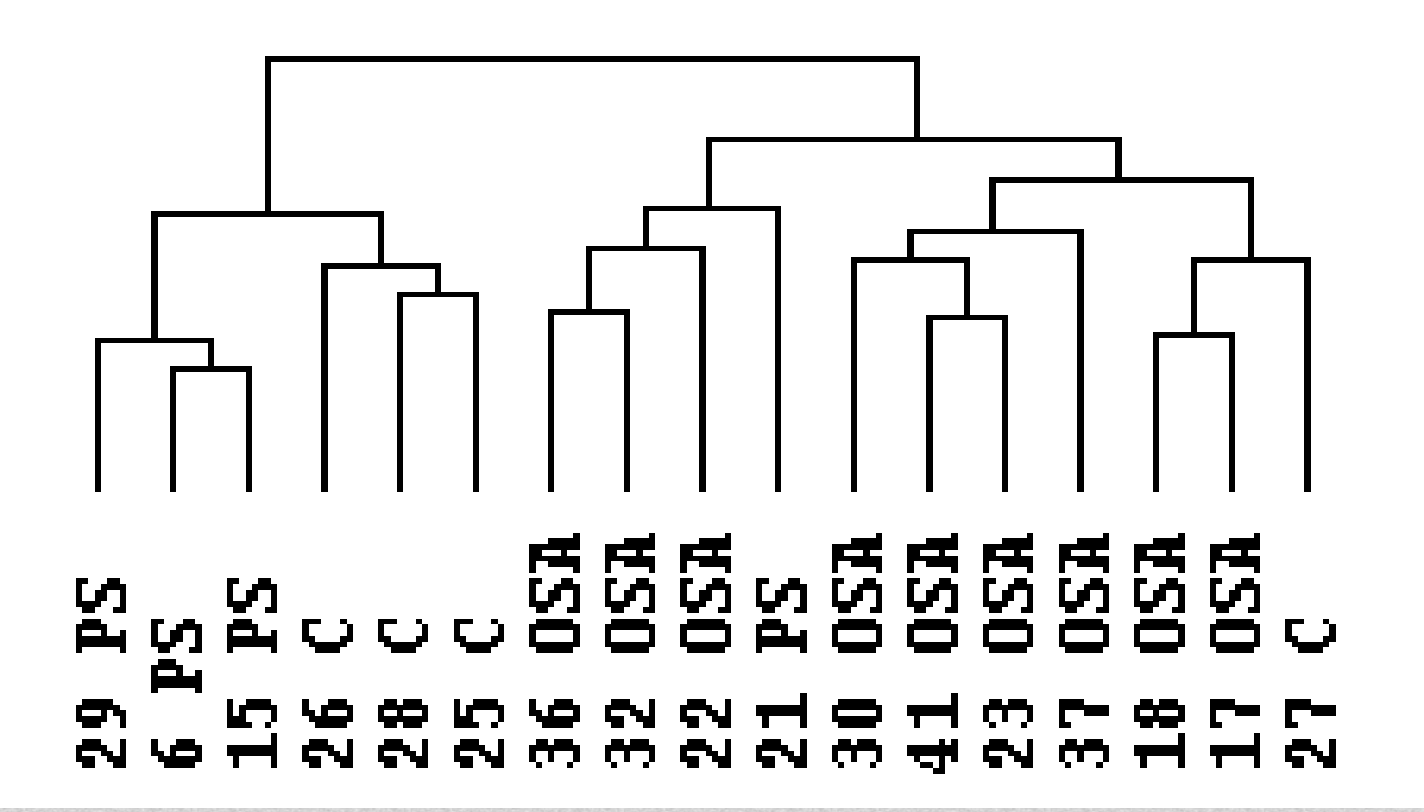
Infogram of gene expression pattern between each group.
Increased expression: brighter yellow
Decreased expression: darker blue

Only genes that have false discovery rate <0.01

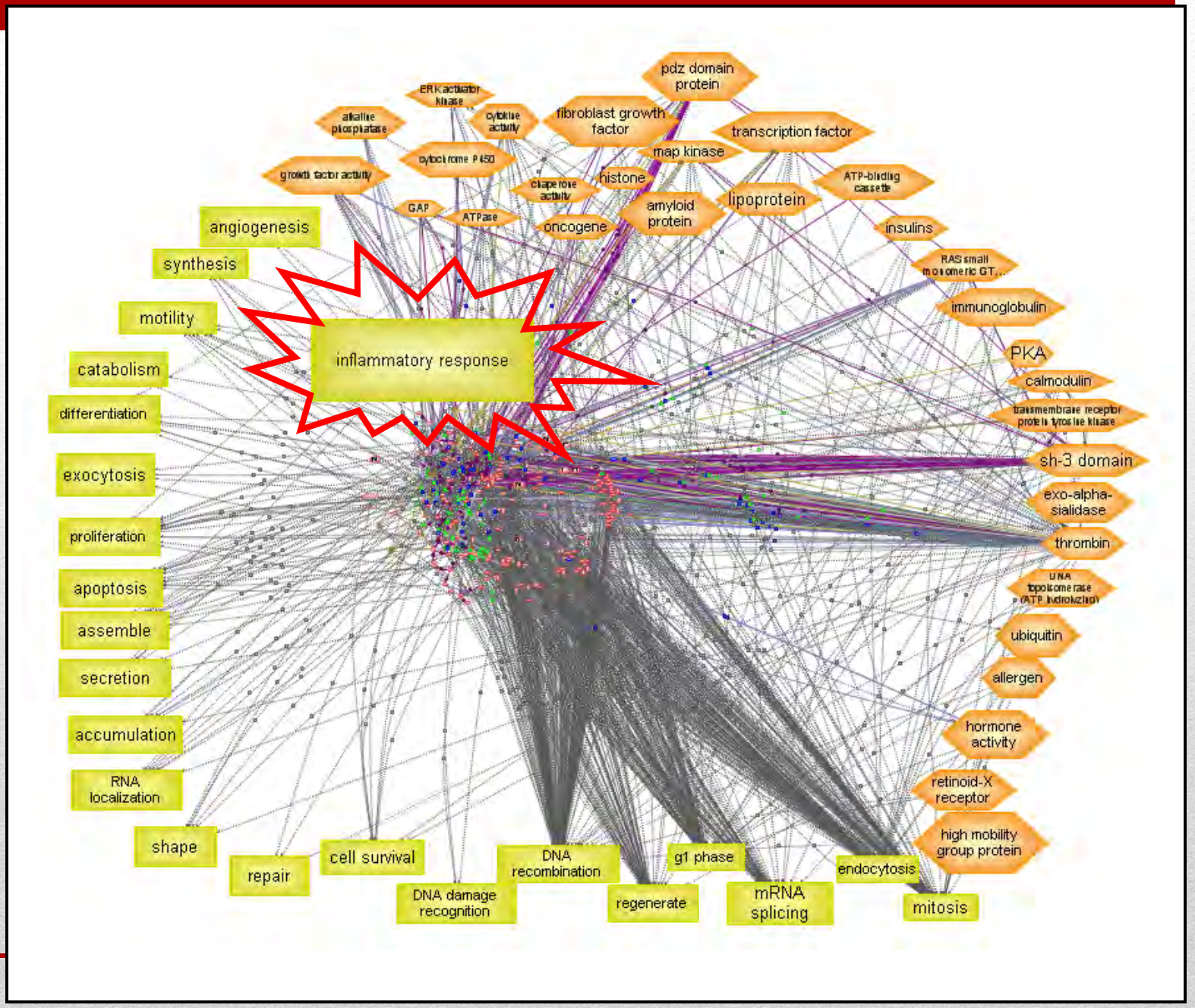
Quantitative RT- PCR was performed on selected genes: agreement with the microarray results

Gozal et al, Thorax 2014

Hierarchical clustering of all the experiments.
Using genes that had at least a FDR <0.01 in TNoM (242 genes)



Gozal et al, Thorax 2014



Khalyfa et al, Sleep Medicine, 2009

SCIENTIFIC INVESTIGATIONS

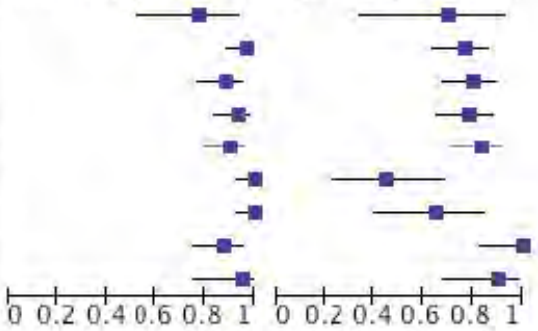
JCSM
Journal of Clinical Sleep Medicine

pii: jc-00272-14
http://dx.doi.org/10.5664/jcsm.4358

Diagnostic Capability of Biological Markers in Assessment of Obstructive Sleep Apnea: A Systematic Review and Meta-Analysis

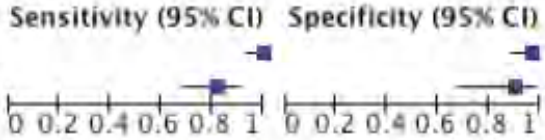
A

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Benedek et al	14	3	4	7	0.78 [0.52, 0.94]	0.70 [0.35, 0.93]
Gozal et al (1)	58	14	2	46	0.97 [0.88, 1.00]	0.77 [0.64, 0.87]
Gozal et al (2)	53	12	7	48	0.88 [0.77, 0.95]	0.80 [0.68, 0.89]
Gozal et al (3)	56	13	4	47	0.93 [0.84, 0.98]	0.78 [0.66, 0.88]
Gozal et al (4)	54	10	6	50	0.90 [0.79, 0.96]	0.83 [0.71, 0.92]
Kheirandish-G et al (1)	50	11	0	9	1.00 [0.93, 1.00]	0.45 [0.23, 0.68]
Kheirandish-G et al (2)	50	7	0	13	1.00 [0.93, 1.00]	0.65 [0.41, 0.85]
Kheirandish-G et al (3)	44	0	6	20	0.88 [0.76, 0.95]	1.00 [0.83, 1.00]
Shah et al	19	2	1	18	0.95 [0.75, 1.00]	0.90 [0.68, 0.99]



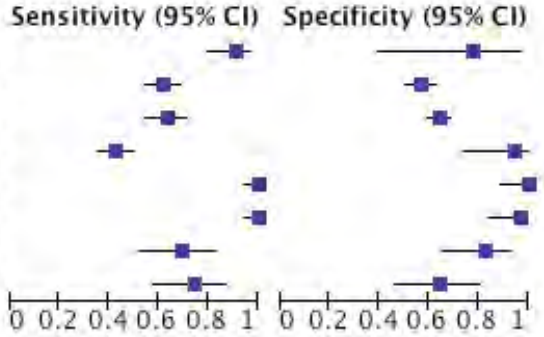
B

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Gozal et al	60	2	0	58	1.00 [0.94, 1.00]	0.97 [0.88, 1.00]
Kheirandish-Gozal	41	2	9	18	0.82 [0.69, 0.91]	0.90 [0.68, 0.99]



C

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Guo et al	49	2	5	7	0.91 [0.80, 0.97]	0.78 [0.40, 0.97]
Hiortsu et al (1)	119	114	73	150	0.62 [0.55, 0.69]	0.57 [0.51, 0.63]
Hirotsu et al (2)	93	150	54	268	0.63 [0.55, 0.71]	0.64 [0.59, 0.69]
Lentini et al	78	1	104	18	0.43 [0.36, 0.50]	0.95 [0.74, 1.00]
Li et al (1)	68	0	0	32	1.00 [0.95, 1.00]	1.00 [0.89, 1.00]
Li et al (2)	68	1	0	31	1.00 [0.95, 1.00]	0.97 [0.84, 1.00]
Ursavas et al (1)	27	6	12	28	0.69 [0.52, 0.83]	0.82 [0.65, 0.93]
Ursavas et al (2)	29	12	10	22	0.74 [0.58, 0.87]	0.65 [0.46, 0.80]



(**A**) Studies in children that analyzed each biomarker individually. (**B**) Studies in children that combined three or four biomarkers in one analysis. (**C**) Studies in adults. TP, true positive; FP, false positive; FN, false negative; TN, true negative.

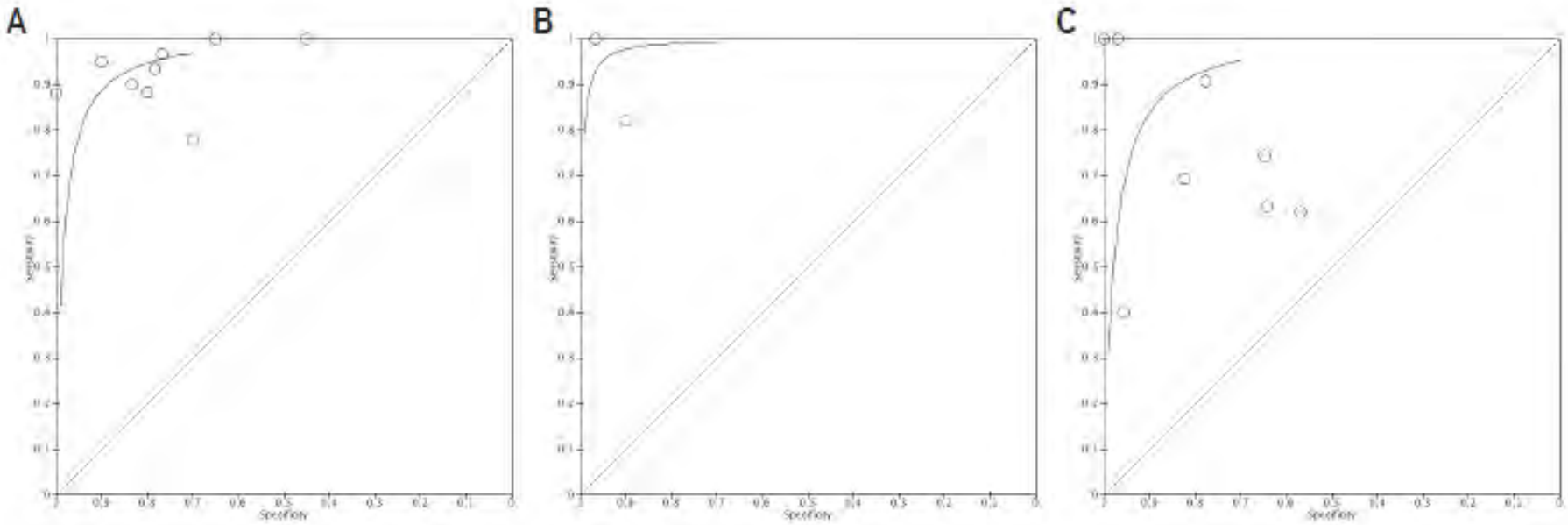
SCIENTIFIC INVESTIGATIONS

JCSM
Journal of Clinical Sleep Medicine

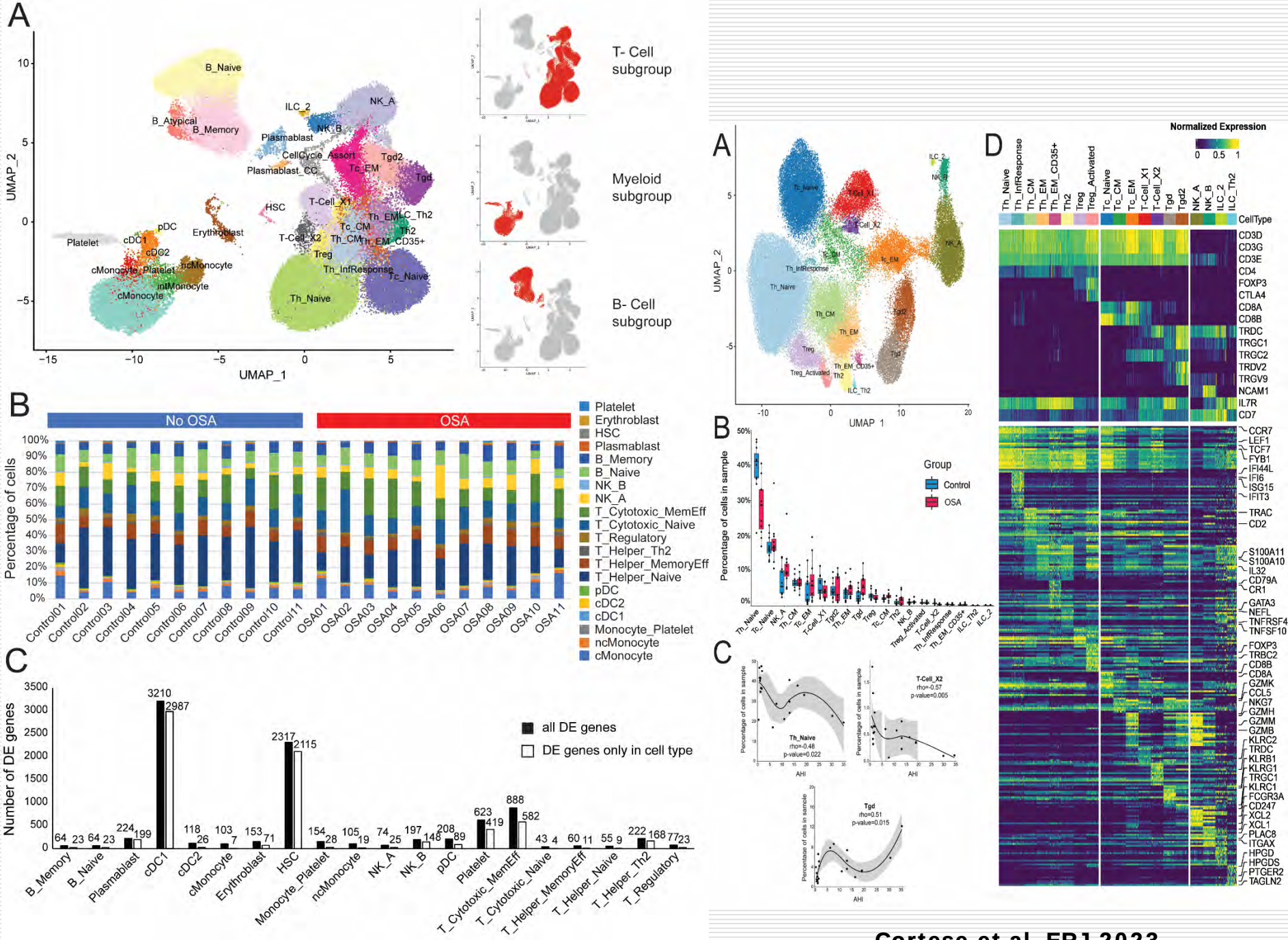
pii: jc-00272-14
http://dx.doi.org/10.5664/jcsm.4358

Diagnostic Capability of Biological Markers in Assessment of Obstructive Sleep Apnea: A Systematic Review and Meta-Analysis

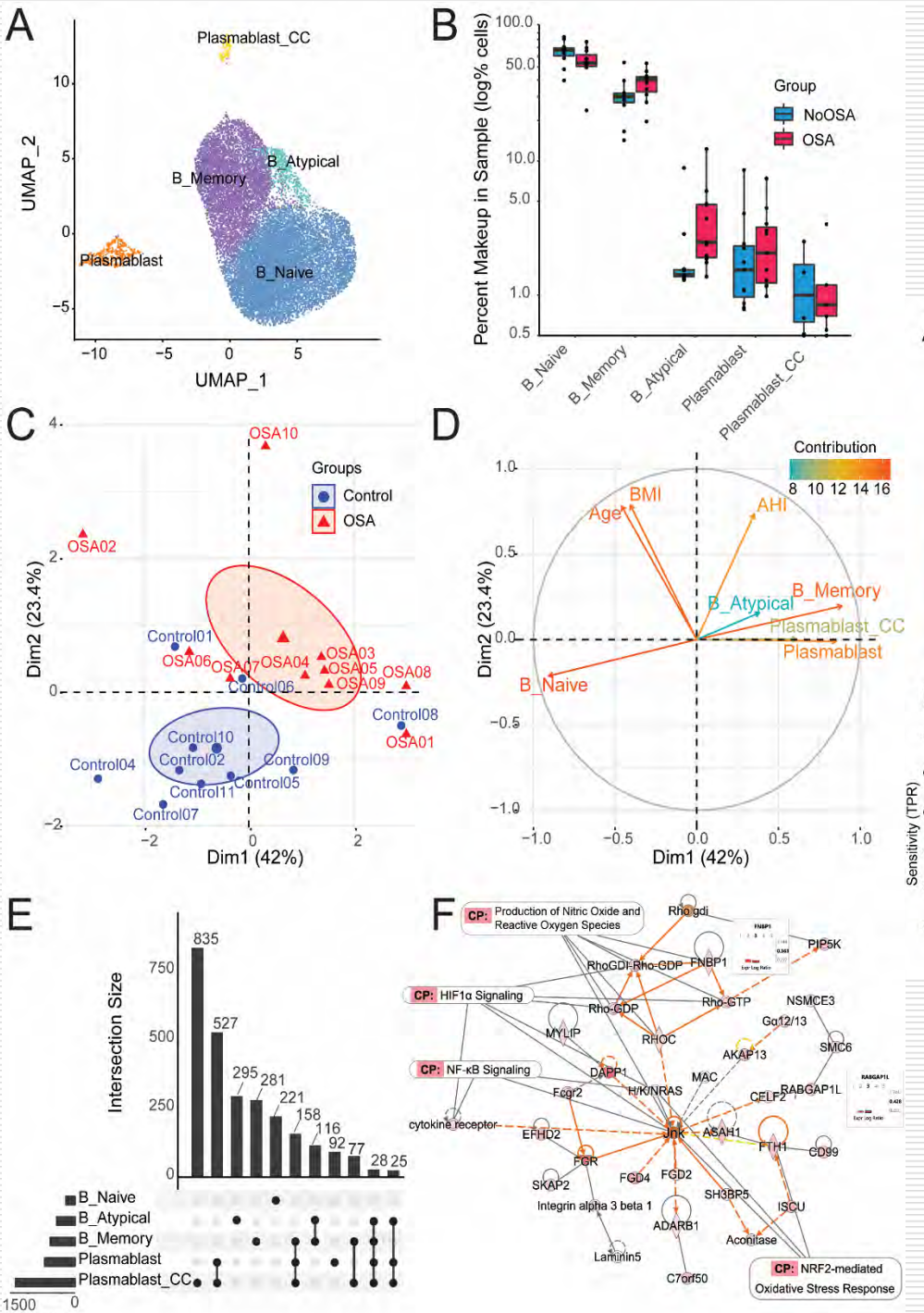
Graziela De Luca Canto, DDS, MSc, PhD[1,2]; Camila Pachêco-Pereira, DDS[2]; Secil Aydinoz, MD[3,4]; Paul W. Major, DDS, MSc, FRCD(C)[2]; Carlos Flores-Mir, DDS, DSc, FRCD(C)[2]; David Gozal, MD[4]

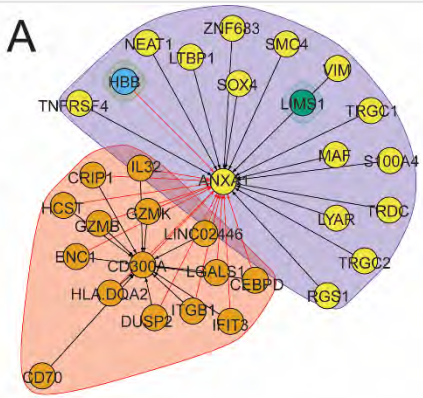


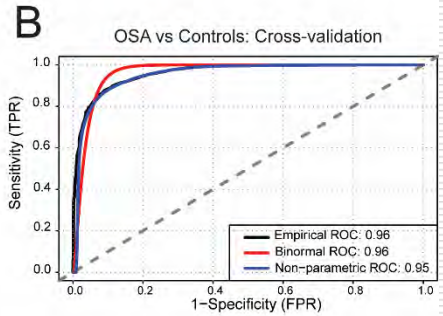
(**A**) Studies in children that analyzed each biomarker individually. (**B**) Studies in children that combined three or four biomarkers in one analysis. (**C**) Studies in adults.

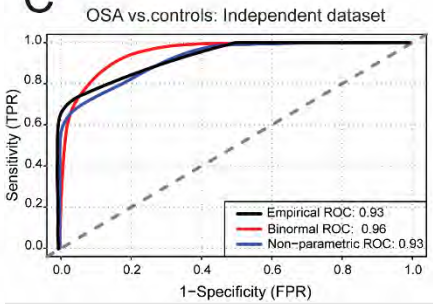


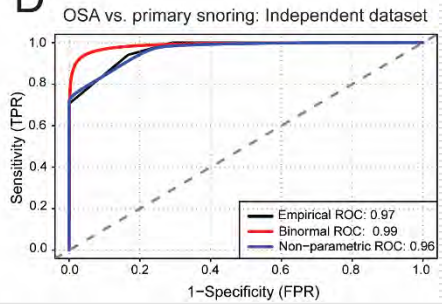
Cortese et al, ERJ 2023











(96% accuracy)

Cortese et al, ERJ 2023

Summary

- The high prevalence of OSA in adult and pediatric populations and the onerous nature of current diagnostic methods make this disease a strong candidate for biomarker-based diagnostic or screening approaches.
- Since only a proportion of OSA patients exhibit end-organ morbidity, which is usually not routinely assessed in clinical practice, biomarkers may offer opportunities for risk stratification, prioritization for therapy, and potentially enable more personalized therapeutic algorithms adjusted for resource availability settings.

Pediatric Home Sleep Apnea Testing

Slowly Getting There!

CHEST 2015; 148(6):1382-1395

Hui-Leng Tan, MBBS; Leila Kheirandish-Gozal, MD; and David Gozal, MD, MBA, FCCP

- The scarcity of access to in-laboratory NPSG in children has prompted intense search for alternative methodologies. Four types of home-based methodologies are emerging each fraught with unique advantages and disadvantages, namely first, questionnaires; second, single-channel recordings; third, home-polysomnography (hNPSG) or polygraphy; (hPG) and fourth, biomarkers.
- Questionnaires are useful for screening but are unlikely to provide the requisite diagnostic accuracy.
- Single-channel recordings may substitute initial NPSG assessments and allow for reliable diagnosis of more severely affected patients.
- hNPSG and hPG may transform over time into the gold standard.
- The use of biomarkers for screening, detection of morbidities associated with pediatric SDB, or identification of residual OSA after treatment should be intensely pursued.

CURRENT OPINION

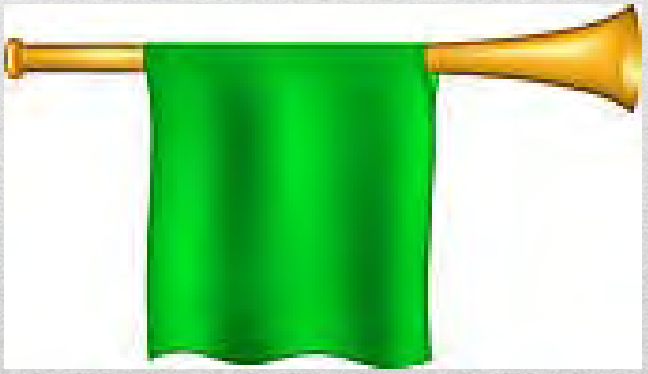
Home sleep testing for the diagnosis of pediatric obstructive sleep apnea: the times they are a changing . . . !

Curr Opin Pulm Med 2015, 21:563–568

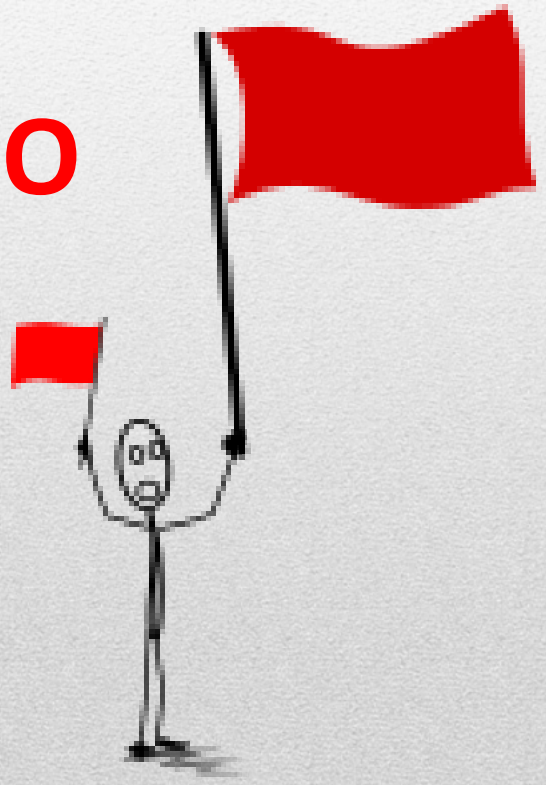
David Gozal[a], Leila Kheirandish-Gozal[a], and Athanasios G. Kaditis[b]

Is a PSG strictly necessary for the diagnosis of OSA in children?

SI



NO



Thank you for your attention!